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The H. K. Cushing Laboratory of Experimental Medicine

EDITED BY
G. N. STEWART, M. D., DIRECTOR

Volume III
1913-1914

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STUDIES ON THE CIRCULATION IN MAN.

VI. OBSERVATIONS ON THE BLOOD FLOW IN THE HANDS (MAINLY) IN CASES OF ANEMIA.*

BY G. N. STEWART, M.D.

(From the H. K. Cushing Laboratory of Experimental Medicine of Western Reserve University, Cleveland.)

Since anemia has a special influence on the blood flow in the peripheral parts, which it is essential to make clear, it has been judged well to begin the description of the results obtained in clinical cases illustrating various diseases with a discussion of the results in the anemias.

The common characteristic of the anemias as regards this point is a small flow in the hands as compared with the normal person of similar age and under similar external conditions. Thus in H. W., the flow was only 2.06 grams per 100 cubic centimeters of hand per minute for the right hand, and 1.82 grams for the left; *i. e.*, only one third to one sixth the amount to be expected in a healthy man.

H. W., a man aged 24 years, was admitted to Lakeside Hospital, suffering from pernicious anemia. Face and hands pale. Erythrocyte count 2,000,000,

Time.	Temperature of calorimeters.		Notes.
	Right.	Left.	
3.08	30.16°	30.21°	
3.10	30.15°	30.19°	Room temperature 23.5° C.
3.11	30.16°	30.20°	
3.12	30.17°	30.20°	Room temperature 23.4° C.
3.13	30.17°	30.21°	
3.14	30.17°	30.21°	Ears pale
3.15	30.18°	30.22°	
3.16	30.19°	30.21°	Room temperature 23.6° C.
3.18	30.20°	30.22°	
3.19	30.19°	30.22°	
3.21	30.20°	30.22°	Room temperature 23.6° C.
3.23	30.21°	30.22°	
3.25	30.22°	30.22°	
3.26	30.22°	30.22°	
3.27	30.23°	30.22°	
3.27½	30.23°	30.22°	
3.39	30.10°	30.09°	

Cooling of calorimeters 0.13° in 11½ min. Volume of right hand 412 c.c., of left 378 c.c. Water equivalent of right calorimeter and contents 3,425, of left and contents 3,397.

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* Received for publication, April 28, 1913.

hemoglobin 45 per cent. (April 16, 1911). Before death (May 2, 1911) the erythrocytes fell to 700,000. The hand flow was examined on April 19, 1911. Pulse (sitting) 120, and weak. Mouth-temperature 37.35° C. The hands were put into the bath at 2.58 P.M., into calorimeters at 3.09 P.M., and taken out of the calorimeters at 3.27. 3,015 c.c. of water were in each calorimeter in all hand observations, unless otherwise stated.

Four months earlier the patient had an attack of erysipelas. The flow in the distal half of the right hand was 8.48 grams per 100 cubic centimeters of hand per minute, whereas in a healthy young man (M. C.) of the same age the flow in the distal half of the right hand was 20.77 grams. It has already been pointed out (1) that the flow in the distal part of the hand is decidedly greater than in the whole hand. Since a larger portion of M. C.'s hand was in the calorimeter in this experiment than of H. W.'s, the discrepancy is greater than appears at first sight. It is certain, therefore, that in H. W. in the experiment of December 17, 1910, the flow for the whole hand could not have exceeded four grams per 100 cubic centimeters per minute, notwithstanding the fever and the involvement of the arms in the inflammation.

December 17, 1910. At this time the anemia was well marked (erythrocytes 2,500,000), although less than on admission (November 30, 1910) when the count gave 816,000; hemoglobin 30 per cent. Rectal temperature 38.9° C. As he was too ill to sit up and the foot calorimeters had not yet been constructed, only the distal portion of his right hand was immersed in the bath and calorimeter, it being impossible to immerse the whole hand as he lay in bed. Pulse 112. Hand in bath at 3.18 P.M., in calorimeter 3.28½. 3,050 c.c. water in calorimeter. Room temperature 20.4° C. Hand out of calorimeter at 3.47.

Time.	Temperature of right calorimeter.	Time.	Temperature of right calorimeter.	Time.	Temperature of right calorimeter.
3.27½	28.92°	3.37	28.86°	3.44	29.00°
3.30	28.88°	3.39	28.91°	3.45	29.03°
3.34	28.86°	3.41	28.93°	3.46	29.08°
3.35	28.85°	3.42	28.96°	3.47	29.14°
				4.02	28.98°

Cooling of right 0.16° in 15 minutes. Volume of hand in calorimeter 175 c.c.

In another case of pernicious anemia (D. K.), a man forty-four years old, the flow on an extremely hot day with room temperature 29.1° C. rose to 8.35 grams per 100 cubic centimeters per minute for the right hand, and 8.38 grams for the left, whereas in the normal young man, M. C., already referred to, the flows were respectively 17.98 grams and 16.65 grams with room temperature 27.1° C. In health the flow is not inferior at forty-four years to that at twenty-two. There is of course a cutaneous vasodilatation in response to the high external temperature, otherwise life would be endangered, yet the hand flow in D. K. remains markedly subnormal. It is perfectly intelligible that under these conditions the further reflex vasodilatation under the influence of warm water applied to the contralateral hand is feeble, the flow increasing only to 9.10 grams per 100 cubic centimeters per minute, while the reflex to cold is intense, the flow diminishing to 2.85 grams.

Time.	Temperature of calorimeters.		Notes.	Time.	Temperature of calorimeters.		Notes.
	Right.	Left.			Right.	Left.	
2.25½	31.52°	31.49°	Room temperature 29° C.	2.36	32.02°	31.99°	
2.27	31.53°	31.52°		2.37	32.09°	32.04°	Room temperature 29° C.
2.28	31.58°	31.55°		2.38	32.14°	32.10°	
2.29	31.62°	31.59°	Room temperature 29° C.	2.39	32.20°	32.15°	
2.30	31.665°	31.63°		2.40	32.27°	32.215°	
2.31	31.71°	31.695°		2.41	32.325°	32.27°	
2.32	31.78°	31.74°		2.42	32.39°	32.33°	
2.33	31.83°	31.81°	Room temperature 29.1° C.	2.43	32.42°	32.37°	
2.34	31.895°	31.86°		2.44	32.48°	32.425°	Room temperature 29.3° C.
2.35	31.96°	31.93°					
				2.45	32.52°	32.455°	At 2.45 left hand put in water at 8.1° C.
2.46	32.53°		He feels the water very cold	2.57	32.815°		
2.47	32.54°			2.58	32.85°		
2.48	32.555°		Still feels the water very cold	2.59	32.90°		
2.49	32.585°		The cold water is now at 9° C.	3.00	32.94°		
2.50	32.60°			3.01	32.995°		
2.51	32.62°			3.02	33.03°		
2.52	32.66°		Room temperature 29.2° C.	3.03	33.08°		Room temperature 29.2° C.
2.53	32.71°		He finds the cold water more tolerable	3.04	33.12°		
2.54	32.735°			3.05	33.175°		Hand out of calorimeter at 3.05.
2.55	32.775°		At 2.55 left hand put in water at 43° C.				
2.56	32.795°		Room temperature 29.2° C.	3.23	33.03°		Temperature of left calorimeter is now 32.22° C.

Cooling of right calorimeter in 18 min. 0.145°, of left in 38 min. 0.235°C.

D. K., a blacksmith, 44 years old, was admitted to the City Hospital on July 1, 1912. He complained of shortness of breath, weakness, and buzzing in the ears. His skin had a yellowish cast. Marked anemia. Teeth good but pyorrhea present. There was a loud venous hum in the neck, especially loud on the left side in the sitting posture, and a soft blowing systolic murmur at the apex. Second sound accentuated in pulmonary area. Paresthesia in both extremities (needles and ants). Ophthalmoscopic examination showed stippling of the retina and small miliary hemorrhages in both upper quadrants. X-ray examination negative. Blood examination: erythrocytes 1,648,000, leucocytes 5,400, hemoglobin 45 per cent. The erythrocytes showed marked variation in size; polychromatophilia; punctate basophilic cells; nucleated reds. Diagnosis: pernicious anemia. When the patient was last seen (August 21, 1912) there was no improvement.

July 2, 1912. Hands in bath at 2.14 P.M., and in calorimeters at 2.26½ P.M. Pulse 84 (sitting).

Volume of right hand 480 c.c., of left hand 476 c.c. He is right handed. Water equivalent of calorimeters and contents, right 3,479, left 3,476. Rectal temperature 38.2° C. Blood pressure: systolic 104, 59 (sound gone). Another observation: systolic 102, 61 (sound gone). At 82 the sound suddenly diminished, then increased and again suddenly diminished at 69, to disappear entirely at 61.

In a case of marked secondary anemia (S. K.) the flow was only 1.26 grams per 100 cubic centimeters for the right, and 1.18 grams for the left hand (for the last ten minutes in the calorimeters).

S. K., a woman, aged 48 years, was admitted to the City Hospital on August 26, 1912, with carcinoma of the uterus. She has had a foul smelling discharge from the uterus for a year, with pain in the right iliac region. She has lost greatly in weight. A cauliflower mass can be palpated on the cervix. The skin is pale and anemic. She has suffered from shortness of breath. Blood count on January 26, 1913: erythrocytes 2,112,000, hemoglobin 45 per cent. Died April 9, 1913. No metastases except microscopic ones in the liver.

January 24, 1913. Hands in bath at 3.06 P.M., in calorimeters at 3.16. Mouth temperature 37.15° C. Pulse (sitting) 108.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
3.15	31.32°	31.30°		3.30	31.20°	31.17°	23.4°
3.17	31.29°	31.26°	24.4°	3.31	31.195°	31.165°	23.3°
3.18	31.28°	31.25°	24.4°	3.32	31.19°	31.16°	
3.19	31.275°	31.25°		3.33	31.19°	31.155°	
3.20	31.27°	31.24°	24.4°	3.34	31.18°	31.15°	23°
3.21	31.27°	31.24°	23.9°	3.35	31.18°	31.15°	
3.22	31.26°	31.23°	23.2°	3.36	31.175°	31.14°	23°
3.23	31.25°	31.22°	23.1°	3.37	31.17°	31.135°	23°
3.24	31.24°	31.22°	23.2°	3.38	31.165°	31.13°	23.3°
3.25	31.23°	31.21°	23.3°	3.39	31.16°	31.12°	23.5°
3.26	31.23°	31.20°	23.4°	3.40	31.145°	31.11°	
3.27	31.22°	31.19°	23.5°	3.49	31.035°	31.00°	
3.28	31.21°	31.18°	23.4°				
3.29	31.21°	31.18°					

Hands out of calorimeter at 3.40. Cooling of calorimeters 0.11° C. in 9 min.

Volume of right hand 330 c.c., of left 324 c.c. Water equivalent of calorimeters with contents, right 3,359, left 3,354.

In a young man of twenty-two years (F. W.), the subject of hemophilia, the flow was 5.04 grams per 100 cubic centimeters per minute for the right hand and 3.94 grams for the left (for the last fifteen minutes in the calorimeters) with room temperature at 24.7° C. The flow was scarcely at all increased reflexly by the application of warm water to the contralateral hand, although it was easily decreased in the case of the right hand to 2.79 grams per 100 cubic centimeters per minute by the application of cold water to the left hand. At this time there had been no hemorrhage for six weeks.

Time.	Temperature of			Notes.	Time.	Temperature of		
	Calorimeters.		Room.			Calorimeters.		Room.
	Right.	Left.				Right.	Left.	
2.30	31.38°	31.34°			2.45	31.495°	31.40°	
2.31	31.36°	31.32°	23.2°		2.46	31.515°	31.425°	25°
2.32	31.37°	31.33°			2.48	31.57°	31.455°	25.2°
2.33	31.37°	31.335°	23.3°		2.49	31.59°	31.47°	24.9°
2.34	31.37°	31.335°			2.50	31.60°	31.48°	24.9°
2.35	31.375°	31.34°	23.1°		2.51	31.62°	31.485°	
2.36	31.38°	31.345°			2.52	31.635°	31.49°	24.7°
2.37	31.39°	31.35°	23°		2.53	31.65°	31.495°	
2.38	31.395°	31.355°	22.9°		2.54	31.68°	31.50°	24.4°
2.39	31.40°	31.355°			2.55	31.69°	31.515°	
2.40	31.40°	31.355°	22.5°	Closed window to raise room temperature	2.56	31.695°	31.52°	24.1°
2.41	31.40°	31.36°	22.6°		2.57	31.705°	31.54°	
2.42	31.41°	31.36°			2.58	31.715°		
2.43	31.425°	31.37°	22.7°		2.59	31.725°		24.5°
2.44	31.47°	31.385°			3.00	31.74°		
3.01	31.775°				3.12	31.935°		
3.02	31.795°		24.3°		3.13	31.94°		24.2°
3.03	31.805°				3.14	31.945°		
3.04	31.82°		24.1°		3.15	31.95°		24.3°
3.05	31.84°				3.16	31.945°		
3.06	31.88°		24.0°		3.17	31.945°		24.2°
3.07	31.895°				3.18	31.945°		24.1°
3.08	31.905°			At 3.08 left hand in water at 8° C.	3.19	31.945°		
3.09	31.92°			Left hand begins to ache	3.42	31.68°	31.10°	
3.10	31.925°			Left hand beginning to get red; it was pale in the warm water				
3.11	31.93°							

Cooling of calorimeters, right 0.265° in 23 min., left 0.44° in 44 min.

F. W., an engineer, aged 22 years, was admitted to the City Hospital on October 8, 1912. He stated that he had had rheumatism in the right leg for some time. Twelve days before admission he bumped it against a bench. It became gradually red and swollen, with considerable pain, so that he could not walk. Then the leg became black and blue. It was opened, as it was thought that it might be suppurating, but only a large hematoma, perfectly sterile, was found. He stated that one brother died of bleeding after a tooth had been pulled. An uncle on his mother's side bled to death from the nose. He did not know of any hemophilic cousins. A grandfather and grandmother were cousins. At seven years of age he cut his hand and almost bled to death. After a cut on the foot he bled for several days. The gums and nose bleed occasionally for two or three days at a time, but his nose has not bled for five months. His leg became infected after it was opened and continued to discharge blood and serous liquid. It was treated by injections of horse serum and then of gelatin and gradually healed. On October 25 the blood examination showed the following: erythrocytes 2,376,000; leucocytes 7,200 (polymorphonuclears 61.4, eosinophils 1.6, small mononuclears 20.6, large mononuclears 9.1, transitionals 5.7). On October 31 the erythrocytes were 3,026,000. He was discharged on January 21, 1913, his leg being cured.

December 27, 1912. Hands in bath at 2.20 P.M., in calorimeters at 2.30½ P.M., taken out of calorimeters at 3.19. At 2.57 left hand put into water at 42.8° C.

Volume of right hand 449 c.c., of left 403 c.c. He is right handed. The left hand is noticeably less than the right. The left arm is also distinctly smaller than the right. He attributes this to rheumatism which used to affect the left wrist. Water equivalent of calorimeters with contents, right 3,454, left 3,417. Rectal temperature 37.25° C. Blood pressure: right arm, systolic 124, 73 (sound gone).

In Mrs. M. A., a woman thirty-eight years old, with an erythrocyte count of 3,000,000 and a hemoglobin percentage of 80, the flow was 4.70 grams per 100 cubic centimeters per minute in the right hand, and 5.44 grams in the left hand (for the last thirteen minutes in the calorimeters) with room temperature 23.1° C., a flow below the normal for her age. The tardiness with which the point was reached at which the thermometers began to rise uniformly, indicating stubborn vasoconstriction, illustrates a characteristic of this group of cases.

Mrs. M. A., aged 38 years, was admitted to the City Hospital on January 1, 1913. She has six children and has had no miscarriages. She menstruated last in August. She sometimes misses two or three months, but has never stopped so long before except when pregnant. She complains of pains in the right side about the liver. In July the abdomen became enlarged and the feet swelled. She denies that she has ever used alcohol. On admission she was jaundiced over the entire body. The abdomen was distended and fluid was present in it. Veins over abdomen are engorged. The liver extends to the umbilicus on the right side and three fingers' breadth below the costal margin on the left. The edge of the liver is hard and sharp but no nodules can be felt. The spleen is hard and easily palpable. X-ray examination negative. Wassermann negative. On January 13, 1913, the erythrocyte count was 3,004,000, the leucocyte count 6,600, hemoglobin 90 per cent. On January 23 the erythrocytes were 2,500,000, hemoglobin 80 per cent., leucocytes 7,000 (polymorphonuclear 72 per cent., eosinophils 1 per cent., large mononuclears 9 per cent., small mononuclears 13 per cent., transitionals 4 per cent.). On January 28 the erythrocyte count was 3,600,000; hemoglobin 70 per cent. There was some hematuria all along (albumin in the urine and erythrocytes), also a few casts. Gynecological examination showed nothing abnormal. Examination of the thorax negative. Radial pulse, symmetrical, equal, regular, good volume and tension. No evidence of parasites. The blood flow in the hands was examined on January 28, 1913. On this date she states that she is stronger than when she entered the hospital. She has no pain now. Her lips are red, though the face is somewhat pale. She used to have good color. Her appetite is not very good, but she is not at all emaciated. Blood pressure: systolic 118, 85 (change in sound). Diagnosis: cirrhosis of liver. She was discharged improved on February 19, 1913.

Hands in bath at 2.33 P.M., in calorimeters at 2.45, and out of calorimeters at 3.09. Pulse (sitting) 80. Mouth temperature 36.85° C.

Time.	Temperature of		
	Calorimeters.		Room.
	Right.	Left.	
2.44	31.12°	31.04°	
2.46	31.07°	31.02°	23.1°
2.47	31.07°	31.02°	
2.48	31.08°	31.02°	23.15°
2.49	31.09°	31.03°	
2.50	31.09°	31.03°	23.2°
2.51	31.085°	31.035°	
2.52	31.09°	31.03°	23.2°
2.53	31.09°	31.035°	
2.54	31.09°	31.035°	23.15°
2.55	31.09°	31.04°	
2.56	31.095°	31.04°	
2.57	31.10°	31.05°	23.2°
2.58	31.105°	31.055°	
2.59	31.115°	31.07°	23.1°
3.00	31.125°	31.085°	
3.01	31.15°	31.11°	
3.02	31.17°	31.135°	23.05°
3.03	31.18°	31.15°	
3.04	31.195°	31.165°	23°
3.05	31.20°	31.185°	
3.06	31.21°	31.21°	23.1°
3.07	31.22°	31.225°	
3.08	31.23°	31.24°	23.2°
3.09	31.24°	31.25°	
3.19	31.115°	31.135°	

Cooling of calorimeters in 10 min., right 0.125°, left 0.115°. Volume of right hand 330 c.c., of left 332 c.c.

In three cases of the chlorotic type the flow although probably below the normal was by no means scanty. Thus in E. D., a girl of sixteen years with an erythrocyte count of 4,100,000 and a hemoglobin percentage of 50, the flow in the right hand was 6.25 grams per 100 cubic centimeters per minute, and in the left 5.76 grams (for the last thirteen minutes in the calorimeters) with room temperature 22.2° C. The contralateral vasodilatation produced by warmth was slight; the contralateral vasoconstriction produced by cold was much more distinct.

E. D., a Hungarian girl, aged 16 years, a dispensary patient, has been ill for about six months suffering from shortness of breath on exertion, as in walking. Her appetite was very poor for about nine months, but is now better. For eleven months she worked eight hours a day in a cigar factory and to this she attributes her illness. She is pale, while before her illness she says she had a good color. A venous hum can be heard in the neck. Her hands are rather thin. She has occasional headaches with severe temporal pain. She states that other girls in the factory have become ill in the same way. On February 4, 1913, erythrocyte count 4,100,000, hemoglobin 50 per cent.

The flow in the hands was examined on February 5, 1913. Hands in bath at 2.30 P.M., in calorimeters at 2.40½ P.M. Pulse (sitting) 130, and weak. She had just walked up to the third floor room where the observations were made. Mouth temperature 37° C. At 3.09 P.M. left hand put into water at 43° C., at 3.23 P.M. into water at 8.5° C.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.39	31.08°	31.04°		2.55	31.105°	31.115°	
2.41	31.00°	31.07°		2.56	31.12°	31.12°	22°
2.42	31.00°	31.06°	21.5°	2.57	31.13°	31.135°	22.2°
2.43	31.01°	31.05°		2.58	31.17°	31.17°	22.2°
2.44	31.005°	31.04°	21.5°	2.59	31.195°	31.19°	
2.45	31.01°	31.04°		3.00	31.20°	31.20°	22.25°
2.46	31.01°	31.06°		3.01	31.215°	31.21°	
2.47	31.01°	31.07°	21.6°	3.02	31.23°	31.22°	22.2°
2.48	31.04°	31.075°	21.7°	3.03	31.26°	31.23°	
2.49	31.05°	31.08°		3.04	31.29°	31.24°	
2.50	31.065°	31.09°	21.9°	3.05	31.29°	31.25°	
2.51	31.07°	31.095°		3.06	31.295°	31.26°	22.3°
2.52	31.08°	31.10°	22.1°	3.07	31.30°	31.27°	
2.53	31.095°	31.105°		3.08	31.30°	31.265°	
2.54	31.10°	31.11°		3.09	31.305°	31.26°	22.5°

Time.	Temperature of		Time.	Temperature of		Time.	Temperature of	
	Right calorimeter.	Room.		Right calorimeter.	Room.		Right calorimeter.	Room.
3.10	31.31°		3.18	31.395°		3.26	31.49°	22.4°
3.11	31.32°		3.19	31.415°	22.45°	3.27	31.495°	
3.12	31.32°	22.5°	3.20	31.43°		3.28	31.495°	
3.13	31.32°		3.21	31.45°		3.29	31.495°	
3.14	31.325°	22.4°	3.22	31.465°	22.45°	3.30	31.505°	22.4°
3.15	31.34°	22.45°	3.23	31.48°		3.31	31.505°	
3.16	31.365°		3.24	31.48°		3.32	31.505°	
3.17	31.38°		3.25	31.48°	22.5°	3.33	31.54°	Hand out of calorimeters at 3.33. Temperature of left at 3.48, 30.72° C.
						3.48	31.31°	

Cooling of calorimeters, right 0.23° C. in fifteen minutes, left 0.54° C. in thirty-nine minutes. Volume of right hand 303 c.c., of left 275 c.c. Water equivalent of calorimeters with contents, right 3,337, left 3,315. Pulse (sitting) at the end of the examination 96. It is stronger than with the more rapid rate before the examination. Blood pressure in left arm, systolic 105, 73 (sound gone), 85 (sound decreased).

In Mrs. A. P., who was still nursing completely her thirteen months old baby, the red cell count was 4,600,000, the hemoglobin 70 per cent., the flow in the right hand 8.75 grams per 100 cubic centimeters per minute, and in the left hand 8.09 grams with room temperature 23.5° C.

Mrs. A. P., aged 32 years, a dispensary patient, was admitted on February 3, 1913. The face, lips, and sclerotics are anemic. She suffers from shortness of breath on exertion. She has been ill for three weeks. She has had a good deal of trouble with her teeth. She is fairly fat and well nourished. Her feet get very cold up to the knees, but her hands do not get so cold. The physical examination revealed nothing special. On February 3 erythrocyte count 4,600,000, hemoglobin 70 per cent. On February 4 hemoglobin 70 per cent. by Haldane-Gower's hemoglobinometer. Her hands seem well supplied with blood, but it does not ooze very freely from a prick either in the finger or in the ear lobe.

The blood flow in the hands was examined on February 4, 1913. Pulse (sitting) 104, shortly after climbing to the third floor. Hands in bath at 2.22 P.M., into calorimeters at 2.39 P.M., and out of calorimeters at 2.53.

Time.	Temperature of			Time.	Temperature of calorimeters.		Notes.
	Calorimeters.		Room.		Right.	Left.	
	Right.	Left.					
2.38	30.88°	30.81°		2.48	31.14°	31.08°	Room temperature 23.45°.
2.40	30.90°	30.80°					
2.41	30.89°	30.82°	23.2°	2.49	31.16°	31.105°	
2.42	30.89°	30.82°		2.50	31.22°	31.14°	Room temperature 23.5°.
2.43	30.91°	30.84°					
2.44	30.955°	30.90°	23.4°	2.51	31.27°	31.175°	
2.45	31.01°	30.945°		2.52	31.29°	31.20°	
2.46	31.04°	30.99°	23.45°	2.53	31.335°	31.22°	Room temperature 23.6°.
2.47	31.095°	31.035°		3.15	31.10°	30.97°	

Cooling of calorimeters in 22 min., right 0.235°, left 0.25°. Volume of hands, right 390 c.c., left 386 c.c. Mouth temperature 37.0°. Pulse (sitting) at end 88.

Water equivalent of calorimeters with contents, right 3,407, left 3,404. Blood pressure in left arm, systolic 115, 63 (sound gone). Another observation, 114, 62.

In Mrs. T., a woman aged thirty years, with an erythrocyte count of 4,584,000 and a hemoglobin percentage of only 40, the flow in the right hand was 6.48 grams per 100 cubic centimeters per minute, and in the left 7.20 grams, with room temperature 22.6° C.

Mrs. T., aged 30 years, height 5 feet 2 inches, dispensary patient. She has children. She has been treated for falling of the womb. Menses regular. Suffers from weakness, pains in the back, and headache. She easily becomes short of breath. She has not been losing flesh. On January 9, 1911, the erythrocyte count was 4,584,000, hemoglobin 40 per cent.

The blood flow in the hands was examined on January 11, 1911. Hands in bath at 3.30 P.M., in calorimeters at 3.40, and withdrawn from calorimeters at 3.55. 3,150 c.c. of water in each calorimeter.

Time.	Temperature of		
	Calorimeter.		Room.
	Right.	Left.	
3.39	30.36°	30.36°	22.6°
3.42	30.43°	30.39°	
3.43	30.46°	30.40°	
3.44	30.48°	30.41°	
3.45	30.50°	30.43°	
3.46	30.50°	30.46°	
3.47	30.52°	30.48°	
3.48	30.56°	30.51°	
3.49	30.59°	30.56°	
3.50	30.62°	30.60°	
3.51	30.65°	30.62°	
3.52	30.68°	30.65°	
3.53	30.70°	30.68°	
3.54	30.71°	30.69°	
3.55	30.72°	30.70°	
4.14	30.52°	30.53°	23.2°

Cooling of calorimeters in nineteen minutes, right 0.20° C., left 0.17° C. Volume of right hand 275 c.c., of left hand 245 c.c. The left hand is visibly smaller than the right. She is right handed. Pulse (sitting) 72. Mouth temperature 37.6° C. Water equivalent of calorimeters with contents, right 3,450, left 3,426.

In a case of anemia (O. L.) secondary to copious gastric hemorrhage in a man aged thirty-six years, the erythrocyte count was 2,250,000, the hemoglobin percentage 45, the flow in the right hand 7.02 grams per 100 cubic centimeters per minute, and in the left 6.90 grams, with a room temperature of 25.4°. These blood flows are rather small, but very much greater than in H. W. and S. K., where the anemia is associated with much graver general changes than in O. L., whose blood changes are probably at this time conditioned mainly or entirely by the hemorrhage. The contralateral vasodilatation to warmth is good, the flow in the right hand being increased from 7.02 grams to 9.93 grams per 100 cubic centimeters per minute when the left hand is immersed in warm water after the usual preliminary diminution to 5.95 grams. The reaction to cold is fair.

O. L., a man, aged 36 years, height 5 feet, 7½ inches, weight 146 pounds. He is a molder, is married, and has one child. He has heavy work in a hot atmosphere. He has always had good health until now. On April 27, 1911, ten days before admission to the dispensary he vomited a large quantity of blood. Since

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then he has suffered from weakness and shortness of breath, also headache and pain in the ears, relieved by lying down, and some epigastric tenderness. Erythrocyte count 2,250,000, hemoglobin 45 per cent. He entered Lakeside Hospital and reappeared at the dispensary on September 9, 1911. The blood count was now good (erythrocytes 6,000,000, hemoglobin 90 per cent., leucocytes 6,200). A test meal (September 28, 1911) showed free hydrochloric acid 30, fatty acid 54, lactic acid 0. In June, 1912, he was operated on at another hospital. He was told that an ulcer was found and that the stomach adhered to the liver. On May 3, 1913, in Lakeside Hospital an inoperable carcinoma was found at the cardia.

The blood flow in the hands was examined on April 27, 1911. Pulse (sitting) 96. Mouth temperature 37.3° C. Hands in bath at 3.30 P.M., and in calorimeters at 3.40½ P.M.

Time.	Temperature of calorimeters.		Time.	Temperature of right calorimeter.	Notes.	Time.	Temperature of right calorimeter.	Notes.
	Right.	Left.						
3.40	29.36°	29.29°	3.53½	29.99°	Room temperature 25.5°	4.06	30.68°	Room temperature 25.3° C.
3.42	29.39°	29.33°	3.54	30.01°				
3.43	29.42°	29.37°	3.55	30.09°		4.07	30.71°	
3.44	29.47°	29.41°	3.56	30.15°		4.08	30.735°	At 4.08 left hand dried and wrapped in towel.
3.45	29.51°	29.44°	3.57	30.23°	The warm water is now at 40°			
3.46	29.56°	29.50°						
3.47	29.61°	29.54°	3.58	30.31°				
3.48	29.68°	29.63°	3.59	30.38°	At 3.59 put left hand in water at 7.7°	4.09	30.77°	Room temperature 25.3° C.
3.49	29.73°	29.70°						
3.50	29.80°	29.74°				4.10	30.79°	
3.51	29.88°		4.00	30.42°	Left hand put into water at 43° C.	4.11	30.82°	
3.51½		29.82°				4.12	30.88°	
3.52½	29.92°					4.13	30.91°	
			4.01	30.46°	Room temperaature 25.4° C.	4.14	30.98°	Hand out of calorimeter at 4.14.
			4.02	30.49°	Room temperature 25.35° C.	4.22	30.89°	At 4.22 temperature of left is 29.61°.
			4.03	30.52°				
			4.04	30.56°				
			4.05	30.61°				

Cooling of calorimeters, right 0.09° in 8 min., left 0.21° in 30½ min.
Volume of right hand 470 c.c., of left 448 c.c. Water equivalent of calorimeters with contents, right 3,471, left 3,453.

In a case convalescing from scurvy (J. B.), a man in the prime of life, the flow in the right hand was 5.53 grams per 100 cubic centimeters per minute, and in the left 6.30 grams, with room temperature 23.9° C. The vasomotor reflexes were good, the flow in the right hand increasing to 10.47 grams, after a preliminary dip to 2.54 grams for one minute, when the left was immersed in warm water and sinking to 5.66 grams for the first three minutes of immersion of the left hand in cold water. For the two minutes succeeding the first minute of immersion of the left hand in cold water the flow in the right is only 4.68 grams per 100 cubic centimeters of hand per minute.

J. B., a laborer, aged 34 years, a patient at the City Hospital, was recovering from scurvy. There was a history of a very poor diet for a long time, bread and tea for some months with no vegetables or fresh meat. He slept under a saloon counter. There was bleeding from the gums, and his legs showed abundant signs of previous hemorrhages. On admission (March 13, 1912) erythrocyte count was 5,000,000, hemoglobin 60 per cent. March 15, 1912, hemoglobin 60 per cent.

The blood flow in the hands was measured on April 4, 1912. Pulse (sitting) 52. Mouth temperature 36.7° C. Hands in bath at 1.02 P.M., and in calorimeters at 1.15 P.M.

Time.	Temperature of calorimeters.		Time.	Temperature of right calorimeter.	Time.	Temperature of right calorimeter.	Notes.
	Right.	Left.					
1.14½	30.54°	30.53°	1.28½	30.795°	1.42	31.41°	
1.16[1]	30.51°	30.51°	1.30	30.84°	1.43	31.44°	
1.17	30.53°	30.53°	1.31	30.89°	1.44	31.50°	
1.18	30.545°	30.55°	1.32[1]	30.93°	1.45	31.52°	
1.19	30.56°	30.57°	1.33	30.99°	1.46	31.56°	
1.20	30.575°	30.605°	1.34	31.06°	1.47	31.595°	At 1.47 left hand dried and wrapped up.
1.21[1]	30.595°	30.625°	1.35	31.12°	1.48	31.62°	
1.23	30.66°	30.70°	1.36[3]	31.18°	1.49	31.63°	
1.24	30.70°	30.74°	1.37	31.21°	1.50	31.69°	
1.25	30.72°	30.79°	1.38	31.225°	1.51	31.74°	
1.26	30.75°	30.82°	1.39	31.24°	1.52	31.79°	At 1.52 hand out of calorimeter.
1.27[2]		30.84°	1.40	31.28°			
1.27½	30.79°		1.41	31.36°	2.04	31.63°	At 2.04 temperature of left is 30.46°.

Cooling of calorimeters: right 0.16° C. in twelve minutes, left 0.38° in thirty-seven minutes. Volume of right hand 407 c.c., of left 410 c.c. He said he was left handed, and the slight preponderance in volume of the left hand bore this out, although as he only spoke Slovak it was difficult to be quite sure. The left hand had more calluses than the right. Pulse (sitting) at end of examination 60. Rectal temperature 37.1° C. Water equivalent of calorimeters with contents, right 3,421, left 3,423.

Finally, in a case of severe nosebleed (G. L.) in a man twenty-six years old, otherwise in good health and without symptoms, the flow was normal (10.27 grams per 100 cubic centimeters per minute for the right hand, and 10.40 grams for the left) with room temperature 24.2° C. The erythrocyte count was 4,256,000.

[1] Room temperature 23.9° C.

[2] Left hand put into water at 42.5° C.

[3] Left hand put into water at 9° C.

G. L., a man, aged 26 years, height 5 feet, 1½ inches, a laborer, was admitted to the City Hospital on November 6, 1912. He complains of bleeding from the nose and sometimes from the gums. This is the second nosebleed he has had. It began on November 3 and continued for some days, stopping and starting again at irregular intervals. He never suffered from hemorrhage from the nose except on these two occasions. No family history of hemophilia. His gums are anemic and spongy in the anterior portion. Pyorrhea alveolaris is present. Teeth fairly good, though neglected. Physical examination of the chest negative. The edge of the liver is palpable, otherwise examination of the abdomen is negative.

The blood flow in the hands was measured on November 7, 1912. His nostrils were plugged with cotton and the bleeding had almost stopped. He walked into the room. Hands in bath at 2.38 P.M., in calorimeters at 2.47¾ P.M., and out of calorimeters at 3.02. Pulse (sitting) 112.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.47	31.635°	31.52°		2.56	31.86°	31.755°	
2.49	31.63°	31.53°	24.2°	2.57	31.90°	31.81°	24.2°
2.50	31.65°	31.54°	24.15°	2.58	31.95°	31.87°	
2.51	31.66°	31.55°	24.1°	2.59	32.00°	31.94°	24.3°
2.52	31.68°	31.57°		3.00	32.08°	31.98°	
2.53	31.71°	31.60°	24.15°	3.01	32.11°	32.04°	24°
2.54	31.76°	31.655°		3.02	32.17°	32.08°	
2.55	31.80°	31.695°	24.1°	3.16	31.98°	31.895°	

Cooling of the calorimeters in fourteen minutes, right 0.19° C., left 0.185° C. Volume of right hand 362 c.c., of left 360 c.c. Water equivalent of calorimeters with contents, right 3,385, left 3,383. Rectal temperature 38.7° C. Blood pressure, right arm, systolic 127, 84 (sound gone). Another observation, systolic 128, 110 (sound suddenly diminished), 86 (sound gone).

Plesch (2) has stated that the output of the left ventricle per minute (the minute volume), measured by a gasometric method, is increased in the cases of anemia investigated by him, including pernicious anemia, chlorosis, and secondary anemias. His explanation is that the deficiency of hemoglobin entails the circulation of a greater quantity of blood through the lungs in order that the oxygen requirement of the body may be filled. He does not discuss the mechanism by which this necessary increase in the minute volume is obtained. My observations on the hand flow indicate in an interesting manner that an important, if not the sole, way in which the increased minute volume of the heart is rendered possible is the diminution in the flow through the periphery by vasoconstriction. This obviously will shorten the average circulation time of the blood and permit its quicker return to the right heart and therefore its more rapid circulation through the lungs. It is to be expected that the cutaneous vessels should be particularly affected by this vasoconstriction. For in the main the blood circulates in the skin, not in the interests of the nutrition of the skin itself, for which a comparatively small flow would suffice, but to regulate the loss of heat. Where it is important that the blood should pass in a fuller stream than ordinary through the lungs it can accordingly be readily spared from the peripheral layers of the body. Since the metabolism in the anemic body is usually less than normal, a smaller cutaneous circulation than normal is in any case required to eliminate the heat produced. If the peripheral vasoconstriction is accompanied by a vasodilatation in the deeper and shorter vascular paths, especially in those passing through the viscera in which a free circulation must be steadily maintained if the metabolism is to proceed normally, the increase in the minute volume of the heart may be all the more easily maintained. Although it may be that the doctrine of reciprocal innervation of the periphery and the deeper parts cannot now be maintained in any very thoroughgoing fashion, there is no question that reciprocal relations can and do exist. The relatively low blood pressure in many of these cases, shows, in so far as it does not depend upon cardiac weakness, that the vasomotor block is not a universal block like that of asphyxia. Where the total volume of the blood is increased, as in chlorosis (3), the increased minute volume of the heart necessitated by the deficiency in hemoglobin may be obtained with little if any diminution in the flow through the skin. For example, if the blood volume were doubled and the hemoglobin percentage halved, the total hemoglobin would be unaltered. It might then be possible that without diminution in the flow through the peripheral parts, the flow through the lungs could be doubled and the oxygen requirement completely met. In this case the quantity of hemoglobin passing through the hand, per unit of time, might be reduced to half without change in the blood flow, while the quantity of hemoglobin passing through the lungs would remain normal. In E. D., for example, the hemoglobin passing through 100 c.c. of hand per minute would correspond only to that contained in three grams of normal blood, a very marked deficiency in the hemoglobin circulation through the hands for a girl of sixteen. In O. L., also, the apparently fair flow of about seven grams of blood per 100 cubic centimeters of hand only corresponds to the hemoglobin of about three grams of normal blood.

In A. P., whose hand blood flow appears to be normal, the hemoglobin going through 100 c.c. of hand per minute is equivalent only to that contained in about six grams of normal blood, a distinct although not a very great deficiency.

We shall not discuss the question whether an increase in the minute volume of the heart in the anemias is not obtained in part or chiefly by an acceleration in its rate. For an increase in minute volume occasioned in this way would equally affect the peripheral circulation unless a redistribution of the blood were brought about by vasomotor action in the manner already suggested. Besides, considerable difference of opinion exists among observers as to the effect of changes in the rate of the heart on its output (4), and as to the changes in the output which are possible. Table I shows clearly that there is no direct relation between the pulse rate and the blood flow through the hand. The highest pulse rate of the series, 120 in H. W., was associated with one of the lowest hand flows, the lowest pulse rate, 52 in J. B., with a fair although subnormal flow. The independence of the hand flow and the pulse rate in different cases is still better displayed in table II, embodying the results on a case of bradycardia, a case diagnosed as paroxysmal tachycardia, a case showing jaundice with a slow pulse, and a case showing jaundice with normal or somewhat accelerated pulse rate.

X., a man, aged 32½ years, height 6 feet, weight 170 pounds. Bradycardia. The first examination of the flow in the hands was made on June 4, 1912. He feels quite comfortable to-day; sometimes he has headaches. He drove his automobile in coming to be examined. He was in the room fifteen or twenty minutes before the observation began. The pulse rate (sitting) was then 37 per minute, on the average of a four minute period. Hands in bath at 1.12½ P.M., in calorimeters at 1.24½, and out at 1.40 P.M. Mouth temperature 36.7° C.

TABLE I.

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature (C.) of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per min.		Flow per 100 c.c. of hand per min.		Notes.
					Room.	Arterial blood.	Calorimeters. Right.	Calorimeters. Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
H.W.	24	Apr. 18, 1911	120		23.5°	37.35°	30.19°	30.20°	412	378	931	753	17	8.49	6.88	2.06	1.82	Pernicious anemia. R. B. C. 2,000,000.
D.K.	44	July 2, 1912	84	103,(82)[4]60	29.1°	37.7°	32.05°	32.03°	480	476	3,670	3,667	18	40.09	39.92	8.35	8.38	Pernicious anemia. R. B. C. 1,648,000. Hemoglobin 45.
							32.54°				191		3	13.70		2.85		Left hand in cold water.
					29.2°		32.67°				957		7	30.20		6.29		Left hand still in cold water.
							32.80°				192		2	21.79		4.54		Left hand in warm water.
							33°				1,478		8	43.67		9.10		Left hand still in warm water.
S.K.	48	Jan. 24, 1913	108		23.3°	37.15°	31.17°	31.14°	330	324	225	208	10	4.18	3.84	1.26	1.18	Carcinoma. R. B. C. 2,112,000. Hemoglobin 45.
F.W.	22	Dec. 27, 1912	100	124,73	24.7°	36.75°	31.55°	31.45°	449	403	1,589	1,145	15	22.63	16.00	5.04	3.94	Hemophilia.
					24.2°		31.80°				1,126		11	22.97		5.11		Left hand in warm water.
					24.2°		31.92°				539		11	11.27		2.79		Left hand in cold water.
M.A.	38	Jan. 28, 1913	80	118,(85)[4]	23.1°	36.85°	31.17°	31.15°	330	332	1,031	1,206	13	15.51	18.08	4.70	5.44	R. B. C. 3,000,000. Hemoglobin 80.
E.D.	16	Feb. 5, 1912	130 96	105,(85)[4]73	22.2°	37°	31.21°	31.19°	303	275	1,285	1,077	13	18.96	15.84	6.25	5.76	Chlorosis. R. B. C. 4,100,000. Hemoglobin 50.
					22.5°		31.32°				320		5	12.51		4.12		Left hand in warm water.
					22.4°		31.40°				930		9	20.50		6.76		Left hand still in warm water.
A. P.	32	Feb. 4, 1913	104 88	115,63	23.5°	37°	31.12°	31.03°	390	386	1,806	1,678	10	34.12	31.23	8.75	8.09	R. B. C. 4,600,000. Hemoglobin 70.
T.	30	Jan. 11, 1911	72		22.6°	37.6°	30.58°	30.55°	275	245	1,466	1,456	13	17.84	17.65	6.48	7.20	R. B. C. 4,584.000. Hemoglobin 40.

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature (C.) of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per min.		Flow per 100 c.c. of hand per min.		Notes.
					Room.	Arterial blood.	Calorimeters. Right.	Calorimeters. Left.	Right.	Left.	Right.	Left	In min.	Right	Left.	Right.	Left.	
O.L.	36	Apr. 27, 1911	96		25.4°	37.3°	29.64°	29.58°	470	448	2,048	1,934	9	33.00	30.93	7.02	6.90	Gastric hemorrhage. R. B. C. 2,250,000. Hemoglobin 45.
					25.4°		29.95°				555		3	27.97		5.95		Left hand in warm water.
					25.4°		30.20°				1,492		5	46.69		9.93		Left hand still in warm water.
					25.4°		30.47°				798		5	25.96		5.52		Left hand in cold water.
					25.3°		30.65°				764		4	31.91		6.79		Left hand still in cold water.
					25.3°		30.86°				1,076		6	30.94		6.58		Left hand dried and wrapped.
J. B.	34	Apr. 4, 1912	52		23.9°	36.7°	30.63°	30.67°	407	410	1,231	1,403	10	22.53	25.85	5.53	6.30	Scurvy.
							30.79°				55		1	10.34		2.54		Left hand in warm water.
					23.9°		30.99°				1,642		7½	42.60		10.47		Left hand still in warm water.
							31.21°				342		3	23.07		5.66		Left hand in cold water.
							31.42°				1,573		8	41.39		10.17		Left hand still in cold water.
							31.61°				205		2	22.37		5.50		Left hand dried and wrapped.
							31.71°				684		3	50.77		12.47		Left hand still wrapped up.
G. L.	26	Nov. 7, 1912	112	128,(110)[4]86	24.2°	38.2°	31.93°	31.83°	362	360	2,098	2,148	10	37.18	37.46	10.27	10.40	Nosebleed. R. B. C. 4,256,000.

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[4] The numbers in brackets are the pressures at which the abrupt decline in the sound occurred; the smaller numbers following are the pressures at which the sound disappeared.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
1.24	31.20°	31.15°		1.33	31.68°[5]	31.70°	
1.25	31.20°	31.17°	24.6°	1.34	31.79°	31.75°	24.6°
1.26	31.27°	31.24°		1.35	31.82°	31.80°	
1.27	31.34°	31.31°	24.8°	1.36	31.87°	31.85°	
1.28	31.395°	31.36°		1.37	31.91°	31.91°	
1.29	31.44°	31.42°		1.38	31.96°	31.95°	24.6°
1.30	31.51°	31.48°	24.7°	1.39	32.01°	32.00°	
1.31	31.58°	31.56°		1.40	32.04°	32.03°	
1.32	31.65°	31.63°		2.04	31.76°	31.755°	

Cooling of calorimeters in twenty-four minutes: right 0.28° C., left 0.275° C. Volume of right hand 493 c.c., of left hand 469 c.c. He is right handed. Pulse (sitting) at end of the blood flow examination 34, average of three minutes. Water equivalent of calorimeters with contents, right 3,489, left 3,470.

Second examination on June 11, 1912. He drove over as on the last occasion. But today his pulse was counted two or three minutes after he came. The rate was 51, average of three minutes. For the first two minutes it was 48 per minute and for the third minute 57. He said that for the last minute he got to thinking about something which constituted a problem for him.

Hands in bath at 1.08 P.M., in calorimeters at 1.19 and out of calorimeters at 1.38. 3,015 c.c. of water in each calorimeter. Mouth temperature 37° C.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
1.18	31.125°	31.04°	24°	1.30	31.65°	31.51°	
1.20	31.18°	31.09°		1.31	31.695°	31.56°	24.6°
1.21	31.24°	31.15°		1.32	31.775°	31.63°	
1.22	31.30°	31.21°	24.6°	1.33	31.86°	31.72°	24.7°
1.23	31.33°	31.235°		1.34	31.90°	31.75°	
1.24	31.39°	31.29°	24.6°	1.35	31.95°	31.79°	24.7°
1.25	31.42°	31.32°		1.36	31.98°	31.82°	
1.26	31.46°	31.35°		1.37	32.01°	31.84°	24.7°
1.27	31.525°	31.405°	24.5°	1.38	32.02°	31.85°	
1.28	31.58°	31.45°		1.55	31.81°	31.65°	
1.29	31.61°	31.47°	24.5°				

Cooling of calorimeters in seventeen minutes, right 0.21°, left 0.20°. Volume of right hand 477 c.c., of left 444 c.c. Pulse (sitting) at end of examination, 34 and 35 in two successive minutes. Water equivalent of calorimeters with contents, right 3,476, left 3,450.

In the first blood flow examination with a pulse rate of 35 the flow in X. was 10.37 grams per 100 cubic centimeters per minute in

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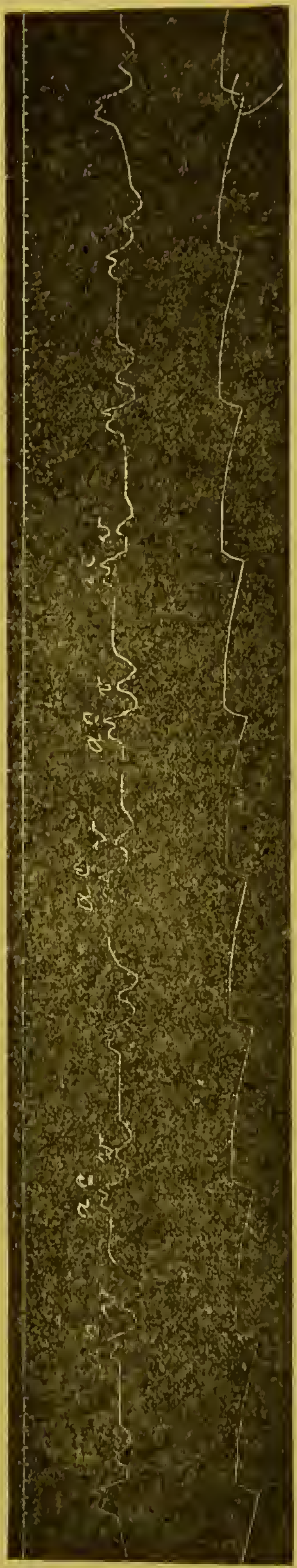
[5] The stirring in the right calorimeter was known to be deficient here.



TEXT-FIG. 1. Part of a polygraph tracing from X., taken May 30, 1912. The lower trace is the radial, the upper the jugular.

the right hand, and 10.93 grams in the left hand, with a room temperature of 24.7° C. A week later, with a somewhat higher average pulse rate and a room temperature of 24.5° C., the flows were respectively 8.75 grams, and 8.32 grams. On the first day he had in accordance with his usual custom for some time taken no lunch, and had rested for a while after coming to the hospital. On the second day he had had lunch and was examined immediately on his arrival. The case was one of true bradycardia, not of heart block, the jugular tracing showing a number of *a* waves equal to the number of beats in the radial artery (text-figure 1).[6]

The patient had been a heavy smoker.

Dr. Carter writes: "He has been under my care since 1907. It was in the spring of 1910 that he had his first syncopal attacks associated with a pulse, at that time of 37 to 42. In the fall of 1910 I sent him to Dr. Thayer in Baltimore for observation." Dr. W. S. Thayer (6) has described this case as one of "permanent bradycardia with no apparent cardiac abnormality. After atropin ($\frac{1}{30}$ of a grain subcutaneously) the pulse rose in twenty minutes to 60. Numerous sphygmographic tracings showed normal auricular and ventricular contractions with no delay in the *a-c* time." April 18, 1913. His pulse rate today is 49 and 46 in two successive minutes. He had just been "running around," he said, so that probably there is no change in rate. The acceleration at the end of inspiration is well marked, as was noted by Dr. Thayer, showing that inhibitory tone is present. A month before he had been operated on for appendicitis under nitrous oxide anesthesia and had made a normal recovery.

In table II is next shown a case (F. R.), a woman aged 52, with a pulse rate of 156 and a blood flow of only 4.78 grams per 100 cubic centimeters per minute for the right hand, and 4.30 grams for the left, although the room temperature was 26° C. This pulse rate indicates complete or almost complete inactivity of the inhibitory mechanism. It is of interest as a sign of concomitant inactivity, as regards reflex changes, of the vasomotor centers that the flow in one hand is practically unaffected by the application of heat or cold to the contralateral hand. So slight a reflex effect as that witnessed in this patient is seldom seen.

Mrs. F. R., aged 52 years, height 5 feet, dispensary patient. Diagnosis "paroxysmal tachycardia." She was never ill until two years ago, when "heart trouble" began. Slight pain in left inframammary region. No enlargement of the heart. No murmurs. Lungs clear. Pharynx reddened. Reflexes normal.

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[6] I am indebted to Dr. E. S. Carter for the tracing, a portion of which is reproduced in the figure, and for the opportunity of studying the case.

TABLE II.

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per mim.		Flow per 100 c.c. of hand per min.		Notes.
							Calorimeters.											
					Room.	Arterial blood.	Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
X.	32½	June 4, 1912	35		24.7°	36.7°	31.62°	31.60°	493	469	3,506	3,531	15	51.12	51.28	10.37	10.93	After rest. No lunch.
		June 11, 1912	51, 35		24.5°	37°	31.60°	31.47°	477	444	3,650	3,312	18	41.72	36.97	8.75	8.32	After lunch, without rest.
F. R.	52	May 25, 1911	156		26°	38.1°	30.12°	30.03°	326	335	1,007	942	9	15.58	14.41	4.78	4.30	
							30.35°				940		8	16.84		5.16		Left hand in warm water.
							30.58°				1,040		10	15.36		4.71		Left hand in cold water.
G.V.	44	Sept. 27, 1912	63	105,69	22.1°	37.1°	31.04°	30.98°	473	467	1,320	1,284	19	12.73	12.27	2.69	2.62	
S.L.	35	Jan. 8, 1913	84	117,80	21.7°	36.75°	31.77°	31.69°	494	467	4,938	4,718	15	73.45	69.06	14.86	14.78	
				(100)[7]	22.4°		32.40°				350		2	44.70		9.05		Left hand in cold water.
					22.2°		32.66°				2,058		8	69.88		14.14		Left hand still in cold water.
					22.1°		33.16°				2,495		10	77.22		15.63		Left hand in warm water.

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[7] The numbers in brackets are the pressures at which the abrupt decline in the sound occurred; the smaller numbers following are the pressures at which the sound disappeared.

She has had thirteen children, nine of whom are alive. She nursed them all. The menopause occurred two years ago. She is corpulent, has shortness of breath on exertion, and attacks of palpitation, especially when excited. Rapid pulse, 165 a minute. No arrhythmia. Three times in the last two years she became unconscious, the first time for two hours. During these attacks her feet, according to her daughter, were quite cold, and were put into hot water. Her hands now feel rather cool, indeed considering the external temperature, quite cool. She has had hard luck and much worry. No thyroid enlargement, no exophthalmos. The symptoms and signs (rapid pulse, increased temperature, and peripheral vasoconstriction) suggest early Graves' disease.

Blood flow in the hands examined May 25, 1911. Mouth temperature 38.1° C. Hands in bath at 2.23 P.M., in calor.meters at 2.33½ P.M. At 2.44 P.M. left hand put into water at 43° C., at 2.52 into water at 9° C.

Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Time.	Temperature of right calorimeter.	Time	Temperature of right calorimeter.	Notes.
2.33	29.95°	29.895°		2.46	30.285°	2.57	30.595°	
2.35	30.005°	29.91°		2.47	30.305°	2.58	30.62°	
2.36	30.35°	29.925°		2.48	30.345°	2.59	30.635°	
2.37	30.06°	29.95°	25.9°	2.49	30.38°	3.00	30.66°	
2.39	30.10°	30.005°		2.50	30.40°	3.01	30.68°	Room temperature 26.1°.
2.40	30.13°	30.025°		2.51	30.43°			
2.41	30.16°	30.04°		2.52[8]	30.46°	3.02	30.695°	Hand out of calorimeter at 3.02.
2.42	30.19°	30.095°		2.53	30.48°			
2.43	30.21°	30.11°	26.1°	2.54	30.495°	3.03		Left 30.03°.
2.44	30.24°	30.135°		2.55	30.53°	3.15	30.60°	Left 29.94°.
2.45	30.27°			2.56	30.57°			

Cooling of calorimeters, right 0.095° in 13 min., left 0.195 in 31 min., 0.09° in 12 min. Volume of right hand 326 c.c., of left 335 c.c. Hands are fat. Pulse 156 (sitting).

The third case in table II, G. V., a man 44 years old, with long standing jaundice and a pulse rate of 63, had a flow in the right hand of only 2.69 grams per 100 cubic centimeters per minute, and in the left 2.62 grams, with room temperature 22.1° C. Anemia was probably a factor in the small peripheral flow. His hands were always cold to the touch. Whether the itching of the skin of which he complained was concerned in the vasoconstriction is unknown.

G. V., a man, aged 44 years, a Hungarian laborer, was admitted to the City Hospital on September 24, 1912. He came in for treatment of a left inguinal hernia which he has had for four years. He also sought the hospital on account of weakness. He is married but has no children. His wife has had no miscarriages. He has had general jaundice for the past eight years. Examination of thorax negative. Liver enlarged, left lobe palpable three fingers' breadth above the umbilicus. Spleen enlarged to percussion, palpable and tender. Skin itches considerably.

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[8] Although the cold water was purposely made one degree higher than usual, she feels it very uncomfortable and complains of it. Her hand had to be taken out of the cold water intermittently for the first 2 or 3 minutes.

Blood flow in hands measured September 27, 1912. Hands in bath at 2.49 P.M., in calorimeters at 2.59, and out of calorimeters at 3.25.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.57½	31.03°	30.98°		3.14	31.00°	30.95°	22.1°
3.00	30.99°	30.94°		3.15	31.01°	30.96°	
3.01	30.98°	30.93°		3.16	31.015°	30.96°	
3.02	30.97°	30.925°		3.17	31.02°	30.965°	22°
3.03	30.97°	30.92°		3.18	31.025°	30.975°	
3.04	30.96°	30.92°	22.1°	3.19	31.04°	30.98°	
3.06	30.96°	30.91°		3.20	31.06°	30.995°	22.2°
3.07	30.96°	30.91°		3.21	31.08°	31.01°	
3.08	30.96°	30.91°	22.3°	3.22	31.09°	31.02°	
3.09	30.965°	30.905°		3.23	31.095°	31.04°	22.2°
3.10	30.97°	30.91°		3.24	31.10°	31.05°	
3.11	30.98°	30.92°	22.2°	3.25	31.10°	31.045°	
3.12	30.99°	30.93°		3.54	30.73°	30.685°	
3.13	30.995°	30.945°					

Cooling of calorimeters in twenty-nine minutes, right 0.37° C., left 0.36° C. Pulse (sitting) 63. Volume of right hand 473 c.c., of left hand 467 c.c. Rectal temperature 37.6° C. Blood pressure, left arm, systolic 104 (palpation), 105 (stethoscope), 69 (sound gone). Another observation: 105, 69. Water equivalent of calorimeters with contents, right 3,473, left 3,469.

In S. L., a case of jaundice with a normal pulse rate, or perhaps a rate somewhat accelerated, the flow in the hands was even greater than normal for the room temperature of 21.7° C.,—14.86 grams per 100 cubic centimeters per minute for the right hand, and 14.78 grams for the left. An increase in the hand flow in disease is much less common than a decrease. The vasomotor reflexes were marked. The increased vasodilatation in the right hand (whose blood vessels must have been already considerably dilated) on immersing the left hand in warm water is especially notable. The flow increased to 15.63 grams per 100 cubic centimeters per minute. Immersion of the left hand in cold water caused a transient diminution of the flow in the right (to 9.05 grams for the first two minutes) followed by an increase to 14.14 grams per 100 cubic centimeters per minute for the remaining eight minutes.

S. L., aged 35, a Slovak, was admitted to the City Hospital on January 1, 1913. He has been sick for two months with pain in the stomach and weakness, but he has not vomited. Never any blood in the stools. He has lost weight to a considerable extent in the past two months, during which he has worked at the National Carbon Works. He has had a cough and several nosebleeds. For the past six or seven months he has been getting more and more jaundiced, but since he entered his present employment the jaundice has been increasing rapidly. He used to drink whiskey moderately. Physical examination of chest and heart shows nothing special. Pulse regular, good tension, good volume, some sclerosis. The abdomen is very rigid and distended. The liver is enlarged, extending to the umbilicus, hard to the touch, not tender. No nodules present. The spleen is also enlarged to the umbilicus and hard but not tender or nodular. A space can be defined between the liver and spleen. Examination of the kidneys negative. Some fluid present in the abdomen. Blood examination: leucocytes 8,000 (polymorphonuclears 69.6, eosinophils 2.6, large mononuclears 3.1, small mononuclears 21.8, transitionals 0.8). The color of the skin, etc., is yellow, not greenish. Diagnosis: hypertrophic biliary cirrhosis.

Blood flow in the hands examined on January 8, 1913. Hands in bath at 2.38 P.M., in calorimeters at 2.49, and out of calorimeters at 3.25. Pulse (sitting) 84. At 3.06 P.M. left hand put into water at 8° C. He feels it very cold. At 3.15 P.M. left hand put into water at 43° C.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.47½	31.13°	31.07°					
2.50	31.17°	31.12°		2.58	31.82°	31.74°	21.8°
2.51	31.24°	31.19°		2.59	31.895°	31.81°	
2.52	31.325°	31.27°		3.00	31.97°	31.88°	22°
2.53	31.415°	31.36°	21.2°	3.01	32.06°	31.96°	
2.54	31.50°	31.43°	21.3°	3.02	32.14°	32.05°	21.8°
2.55	31.58°	31.50°	21.4°	3.03	32.22°	32.13°	
2.56	31.66°	31.58°	21.5°	3.04	32.28°	32.19°	
2.57	31.73°	31.66°		3.05	32.36°	32.26°	
3.06	32.39°		22.4°	3.16	32.935°		22.1°
3.07	32.43°			3.17	32.98°		
3.08	32.495°		22.4°	3.18	33.03°		22.2°
3.09	32.56°			3.19	33.09°		
3.10	32.61°		22.2°	3.20	33.14°		22.2°
3.11	32.67°			3.21	33.20°		
3.12	32.72°		22.15°	3.22	33.26°		22°
3.13	32.79°			3.23	33.32°		
3.14	32.84°		22.2°	3.24	33.38°		22.2°
3.15	32.89°			3.25	33.435°		
				3.40	33.18°	31.75°	

Cooling of calorimeters, right 0.255° in fifteen minutes, left 0.51° in thirty-five minutes. Volume of right hand 494 c.c., of left 467 c.c. Blood pressure, left arm, systolic 117 (palpation), 117 (stethoscope), 80 (sound gone). The sound became indistinct a little below 100, but did not actually disappear till about 80.

The veins of the arms are large. Both hands feel warm to the touch and equally so. The whole skin is warm. Rectal temperature 37.27° C. Water equivalent of calorimeters with contents, right 3,490, left 3,469.

In conclusion it should be pointed out, perhaps, that if in anemia peripheral vasoconstriction, especially in the cutaneous vessels, is a compensatory mechanism for increasing the stream of blood in the lungs, disorders of the skin caused or perpetuated by deficient circulation are rationally treated by measures which augment the hemoglobin content of the blood. When the deficiency of hemoglobin is remedied the deficiency in the cutaneous blood flow will take care of itself. It has long been known and is a commonplace of practice that many skin conditions are benefited by general treatment of the coëxisting anemia where local treatment alone is inefficacious. Local treatment of limited portions of the skin, however, aimed at increasing the blood flow in that region would not be contraindicated from the point of view of the compensatory action of a general peripheral vasoconstriction. For vasodilatation in a limited area of the skin, while it might greatly benefit the local condition, would not appreciably affect the pulmonary flow.

Where anemia is excluded it is probable that the hand flow under standard conditions which eliminate as far as possible accidental local vasoconstriction is an index to the minute volume of the heart, or, rather, gives the means in successive observations of following to some extent changes in the minute volume. This seems to follow from the fact that in one and the same healthy individual and in pathological cases where the clinical state has undergone no sensible change, the hand flow varies only within narrow limits when the subject is under a steady regimen, and the controllable external conditions are the same. The fact then that X., who had no anemia, with a pulse rate of 35, had a hand flow entirely within the normal range for his age may be taken to indicate that his minute volume under the given external conditions was normal. The output per beat must, therefore, have been twice that of a normal man of the same weight. Nothing, of course, can be said from these observations as to the power of his heart to respond to such increased requirements as occur during considerable muscular exertion. Buchanan (7) has remarked that among athletes very slow pulse rates are not incompatible with great exertion.

CONCLUSIONS.

1. In the cases of anemia studied (pernicious anemia, chlorosis, and secondary anemia) the blood flow in the hand is smaller than the normal flow.

2. Accepting Plesch's result, that the minute volume of the heart is increased in the anemias, the diminution in the hand flow is interpreted as a sign of a vasoconstriction in peripheral parts, which facilitates the increased flow through the lungs.

3. The deficiency in the hand flow is less in the chlorotic group than in the other cases of anemia. The explanation suggested is that the increased total volume of the blood in chlorosis permits the normal amount of hemoglobin to circulate through the lungs without a marked increase in the peripheral vasoconstriction.

4. The view that the diminution in the cutaneous blood flow in anemia is a necessary compensatory arrangement for increasing the flow through the lungs affords a natural explanation of the beneficial effect in many cutaneous disorders of general measures, especially those aimed at improving the quality of the blood.

5. In a case of bradycardia with a pulse rate permanently below 40 during rest in a sitting position, the hand flow was normal.

I am indebted to the Staff of Lakeside Hospital and Dispensary, and especially to the Staff of the City Hospital for many courtesies extended to me during this investigation.

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STUDIES ON THE CIRCULATION IN MAN.

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STUDIES ON THE CIRCULATION IN MAN.

VII. THE BLOOD FLOW IN THE FEET.*

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PLATES 22 TO 24.

The calorimetric method already described for the measurement of the flow in the hands[1] was modified to suit the feet. This made it possible to make observations on persons who were too ill to sit in a chair for hand flow measurements.

Since the heat given off by the foot of a normal adult is considerably less than that given off per 100 cubic centimeters of tissue per minute by the hand,[2] it was necessary to construct the interior vessel so that as small an amount of water as possible would suffice to immerse the foot completely.

TECHNIQUE.

In its final form the foot calorimeter consists of an interior oval vessel of tinned copper (figure 1) packed in broken cork in an outer vessel of galvanized iron. Both vessels are somewhat wider at the anterior (toe) end than at the posterior end. The top of the inner vessel has in it an oval opening somewhat wider at the anterior end. This opening, as is obvious from the shape of the foot, must be much larger than in the case of the hand calorimeter, and when the foot has been inserted it is partly closed by the removable copper lid shown at the right lower corner of the figure. The hole in this lid allows it to be lifted easily by the fingers. On the lid, once the foot is in position, lies the thick felt collar shown at the left of the figure. Inside the calorimeter the foot rests on thick copper wire netting, shown leaning against the front of the calorimeter. This allows the water to pass freely under the foot when it is stirred by the two goose feathers, the ends of which are seen protruding from the two openings one on each side of the thermometer. The calorimeter in the figure is tilted so as to display the posterior end of the footrest lying in position on

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[1] Stewart, G. N., *Heart*, 1911, iii, 33.

[2] Stewart, G. N., *loc. cit.*, p. 55.

the bottom of the inner vessel. The anterior part of the top of the inner vessel slants down somewhat towards the front in order to reduce the capacity of the vessel without encroaching on the space needed for the toes. The thermometer is protected against contact with the patient's toes by a cylinder of copper perforated with numerous holes, which passes down through the top of the inner vessel to the level of the lower end of the bulb. The orifice for the introduction of the foot is surrounded by a flange on which the lid and the felt collar rest. Vertical rings of copper surround all the orifices so as to allow the top of the inner vessel to be covered, first with a layer of broken cork, and above that with sheet cork. The upper surface of the sheet cork is varnished. The thickness of the layer of cork over the greater part of the inner vessel is 25 mm., but more in front.

The outer vessel is 260 mm. deep, 225 mm. wide in the middle, and 400 mm. long. The inner vessel is 125 mm. deep below the flange at the posterior (heel end), 135 mm. deep below the flange in the middle, 120 mm. wide in the middle, and 320 mm. long. The length of the orifice at the flange from front to back is 190 mm., the width at the middle 100 mm. The flange is about 8 mm. wide, but a little broader posteriorly. The length of the orifice from front to back when the movable lid is in position is 90 mm., and its breadth 82 mm. The height of the footrest at the heel end is 24 mm., and at the toe end 10 mm.

Figure 2 shows the position of the patient with his feet in the calorimeters when he is well enough to sit in the high chair described in the paper on measurement of the flow in the hand.[3] For the convenience of the observer the chair and the calorimeters are placed upon a platform so as to elevate the thermometers to a sufficient height above the floor to enable them to be read conveniently. By a simple method of fixation all possibility of slipping of the chair is prevented.

In the first experiments a horizontal pencil mark was drawn around the ankle, always bearing the same relation to the external malleolus, and above this a parallel line was drawn at a distance equal to the thickness of the felt collar plus the thickness of the flange. The height of the calorimeters was then adjusted so that the upper line just appeared above the felt collar, the patient sitting in the chair with his legs hanging down. The footrest inside the calorimeter was not used with this arrangement. It was found to be somewhat troublesome for the patient to maintain the same level throughout the experiment in this way. It was therefore decided to abandon it and to cause the patient to set his foot on the footrest. Before withdrawal of the foot a pencil line is now traced around the ankle just below the flange, or it may be traced above the collar, and after withdrawal of the foot a parallel line traced at a distance below the first line equal to the combined thickness of collar and flange. The object of the first procedure was to insure that in all experiments the foot should be inserted into the calorimeter to the same anatomical level, as was always done with the hands. In the case of the hands undoubtedly a fairer comparison of the flow in different individuals is obtained in this way than if the fingers were made in every case to touch the bottom of the calorimeter, since the inclusion of different proportions of the wrist and forearm would to some extent vitiate the results. From the shape of the foot, however, it is clear that the second procedure leads to a much smaller variation in the portion of the foot immersed than would be the case for the hand, since in the adult the variation in the vertical distance from the sole to a given anatomical point on the ankle is much less than the variation of the length of the hand,—from the tip of the middle finger to a fixed anatomical point on the wrist, for example. As a matter of fact, in the adult patients examined the variation in the distance between the flange and a fixed point on the external malleolus when the sole rested on the footrest was small. Any error in comparing the feet of different persons was further reduced by the fact that the difference of level affected the portion of the foot (the ankle) whose horizontal cross section was smallest. For very small feet, as those of children, an additional footrest which increased the space between the sole of the foot and the bottom of the calorimeter was employed. A great advantage of the footrest, in addition to the increased comfort of the patient, is the certainty that without any attention the foot remains at the same level within the calorimeter throughout the experiment. For particular purposes in the case of children or of adults with exceptionally small feet, it may sometimes be desirable, where accurate comparison is required with other cases, to revert to the first method, although of course for comparison of the flow in the feet of one and the same person at different times or under different conditions, this would offer no advantage.

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[3] Stewart, G. N., *loc. cit.*, p. 33.

The volume of the foot was measured by displacement in the same way as that of the hand. The oval copper vessel at the left of figure 2 was made for this purpose. The cross section of the vessel must be as small as possible in order to permit as large a change of level as possible in the attached burette. Where very large or very small feet are being investigated it is of advantage to have vessels of correspondingly different size.

When patients are not well enough to sit up in the chair the flow in the feet can be measured in the way shown in figure 3. The subject is lying on his back on a movable bed with his legs hanging over the foot of the bed. The height of the calorimeters is adjusted so that the soles of the feet rest on the footrest. No complaint of discomfort was made by any of the fever patients investigated in this way.[4]

The technique of the preparatory bath is the same as that for the hands, except that instead of the patient putting his feet into the bath, the bath is generally slipped up over his feet. This is necessarily the case where patients are examined in bed. On account of the greater thickness of the feet, the period of immersion in the bath can advantageously be made longer than is necessary for the hands. For the same reason it is probable that the calculated results differ from the actual flow by a greater amount in the case of the feet than in the case of the hands. In both, of course, the observed flow establishes a minimum below which the actual flow cannot lie. It was pointed out in the previous communication that this follows from the principle of the method.

Another point of considerable importance is that the feet and legs, being less accustomed to exposure than the hands and arms, at least in temperate climates, greater precautions have to be taken to prevent vasoconstriction due to the exposure, especially of wet skin, to the air of the room. The legs are kept

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[4] Stewart, G. N., *Jour. Exper. Med.*, 1913, xviii, 372.

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covered as far as possible down to the bath, and afterwards down to the calorimeters. A somewhat higher bath temperature than that commonly employed for the hands is probably also advantageous for the foot measurements.

In general, measurements of the hand flow are to be preferred for obtaining information as to the condition of the circulation as a whole. It is in cases where the local conditions made it desirable to examine the foot flow, or where the patients were too ill to sit up for the hand examination, that foot flow measurements were undertaken. For the sake of comparison the hand flow was also measured wherever possible. It will be pointed out later that the ratio of the foot flow to the hand flow sometimes reveals interesting features.

The quantity of water put into each calorimeter where the feet are of average size is 2,775 c.c. In the protocols, if no quantity is mentioned, it is always to be understood that this is the amount. In the earlier observations where the capacity of the calorimeters was greater, larger quantities were employed. These are always stated in the protocols. It was afterwards decided to reduce the size of the inner vessels by cutting a segment off the bottom, so that a greater rise of the thermometers might be obtained. This is mentioned to prevent confusion in comparing the results in the earlier and later experiments. The foot volumes are larger in some of the earlier observations than in the later ones because the feet were inserted into the calorimeter to a greater depth. This, however, is not necessarily the case in the experiments in which the feet hung down in the calorimeter, but it is always the case in the experiments made where feet rested on the footrest in the calorimeters before they were reduced in size.

Water Equivalent of the Foot.—A foot was obtained from the body of a well nourished woman, 45 years old, who died of lobar pneumonia. The foot was normal in all respects and was in excellent condition. A tube of skin having been reflected, the leg bones were sawed through at the level which in an average adult foot would be just inside the flange when in position in the calorimeter. The skin was closely stitched around the bone and the line of sutures well covered with melted paraffin, to render the preparation water tight. The foot was slung by means of a thin copper wire in a bath, the temperature of which was kept constant by a regulator. The water was continuously stirred by a mechanical arrangement. The foot was put into the bath at 11.30 A.M. At 12.31 P.M. 3,275 c.c. of water were put into one of the foot calorimeters. At 1.02 P.M. the foot was quickly transferred from the calorimeter after being rapidly wiped with a towel taken out of a thermostat at 38° C., and the rise of temperature in the calorimeter was followed as in the corresponding experiment on the hand.[5]

Time.	Temperature of			Time.	Temperature of	
	Calorimeter.	Air.	Bath.		Calorimeter.	Air.
12.23			37·96°	1.25	18.30°	19.9°
12.28			37·96°	1.27	18.36°	19.8°
12.39	15.69°	18.8°	37·96°	1.29	18.39°	19.8°
12.48	15.80°	18.8°	37·96°	1.31	18.445°	19.7°
12.54	15.85°	18.8°	37·97°	1.34	18.50°	19.7°
1.00	15.895°	18.8°	37·97°	1.37	18.56°	19.7°

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[5] Stewart, G. N., *Heart, loc. cit.*, p. 42.

Time.	Temperature of			Time.	Temperature of	
	Calorimeter.	Air.	Bath.		Calorimeter.	Air.
1.05	17.08°	18.95°		1.41	18.61°	19.6°
1.06	17.22°			1.45	18.665°	19.4°
1.07	17.36°	19.0°		1.50	18.71°	19.5°
1.08	17.46°			1.55	18.755°	19.6°
1.09	17.55°			2.07	18.82°	19.7°
1.11	17.69°	18.95°		2.09	18.83°	19.7°
1.13	17.825°	19.1°		2.21	18.88°	19.5°
1.15	17.92°	19.7°		2.33	18.91°	19.5°
1.17	18.02°	19.7°		2.46	18.935°	19.6°
1.19	18.10°	19.7°		2.56	18.955°	19.5°
1.21	18.175°	19.8°		3.20	18.99°	
1.23	18.235°	19.9°				

Weight of foot, 760 gm. Volume of foot, 717 c.c. The specific gravity of the foot was therefore 1.06. This is less than that of the hand, as determined before, probably because of a considerable amount of fat. After allowance is made for the small amount of heat gained by the calorimeter during the experiment, the specific heat works out at 0.71. The factor by which it is necessary to multiply the volume of a foot in order to obtain its water equivalent is accordingly 1.06 × 0.71, or 0.75.

The temperature of the arterial blood entering the foot was not determined, as it is certain that it cannot differ much from that of the arterial blood at the wrist, which was previously shown in a normal man to be 0.5° C. below the rectal temperature. To allow, however, for the longer path, it was assumed that at the ankle the arterial blood is 0.1° lower than at the wrist. This makes no material difference in any case, but it helps to offset the greater error in the case of the foot involved in the assumption that the venous blood leaving the foot is on the average at the temperature of the calorimeter. From the dimensions of the foot, it is probable that the difference between the temperature of the venous blood at the ankle and that of the calorimeter is greater than the difference between the average temperature of the venous blood at the wrist and that of the calorimeter. Yet in the foot, as in the hand, most of the blood must in some part of its path follow a relatively superficial course.

One point in connection with the calculations, which has, perhaps, not been made clear in the previous paper on the method, although it is sufficiently obvious, may be referred to here, lest a reader in recalculating experiments should be puzzled by small discrepancies. In allowing for the cooling of the calorimeters, the rate of cooling observed at the end of the experiment has been corrected for each period into which the observations are divided, by taking account of the difference of the average temperature of the calorimeter for the given period and the room temperature. Where the total change of temperature of the calorimeters in the whole experiment is small, this correction can be omitted without material error. In no case is the error that is introduced by omitting the correction a great one.

As no results on the feet have hitherto been published, it is necessary, in order to afford a standard of comparison for the pathological cases, to cite some of the results on normal persons. These were obtained on M. C., a man aged 24 years, height 5 feet, 10 inches, weight 165 pounds, on whose hand flow numerous observations had been made; J. R., a man aged 20 years, height 5 feet, 4 inches, weight 125 pounds; C. B., a man aged 24 years, height 5 feet, 8½ inches, weight 130 pounds; and N. R., a boy aged 8 years, 9 months, height 3 feet, 11 inches, weight 54 pounds. The ages are given as at the time of writing of the present paper.

M. C.—May 18, 1911. Right foot put into bath at 2.37 P.M., and into calorimeter at 2.47½. 3,700 c.c. of water in calorimeter. Pulse (sitting) 76. The subject was sitting throughout the experiment, his foot hanging in the calorimeter.

Time.	Temperature of right calorimeter.	Notes.	Time.	Temperature of right calorimeter.	Notes.
2.47	31.17°		2.55	31.42°	
2.49	31.21°		2.56	31.45°	
2.50	31.25°	Room temperature 26.4° C.	2.57	31.48°	
			2.58	31.51°	Room temperature 26.4° C.
2.51	31.27°		2.59	31.535°	
2.52	31.305°		3.00	31.58°	Foot out of calorimeter at 3.00.
2.53	31.34°				
2.54	31.39°		3.16	31.395°	Room temperature 26° C.
			Cooling of calorimeter 0.185° in 16 minutes.		

Volume of right foot in calorimeter (to upper level of external malleolus) 1,210 c.c.

Water equivalent of calorimeter and contents 4,807 c.c. Rectal temperature 37.5° C.

Here with the relatively high room temperature of 26.4° C. the flow per 100 cubic centimeters of foot per minute is 3.54 grams for the right foot, which alone was immersed.

On June 17, 1911, with a considerably lower room temperature (21.8° C.) and a somewhat lower calorimeter temperature, although a higher pulse rate, the flow was higher (4.93 grams for the right and 4.24 grams for the left foot).

June 17, 1911. Feet put into bath at 1.29 P.M. and into calorimeters at 1.40 P.M. 3,700 c.c. of water in each calorimeter. Room temperature 21.8° C. The examination was made in a very large room with the windows closed, so that the temperature was practically constant throughout, and was exactly 21.8° C. at the beginning and at the end of the experiment.

Time.	Temperature of calorimeters.		Time.	Temperature of calorimeters.		Notes.
	Right.	Left.		Right.	Left.	
1.39	30.20°	29.93°	1.49	30.58°	30.245°	
1.42	30.24°	29.98°	1.51	30.69°	30.37°	Better stirring.
1.43	30.28°	30.00°	1.52	30.73°	30.40°	
1.44	30.33°	30.04°	1.53	30.80°	30.43°	
1.45	30.37°	30.085°	1.54	30.84°	30.49°	
1.46	30.42°	30.10°	1.55	30.91°	30.52°	Feet out of calorimeters at 1.55.
1.47	30.46°	30.18°				
1.48	30.53°	30.225°	2.11	30.63°	30.27°	

Cooling of calorimeters in sixteen minutes, right 0.28° C., left 0.25°. Pulse (sitting) 84. Rectal temperature 37.6° C. Water equivalent of calorimeters with contents, right 4,777 c.c., left 4,714 c.c. Volume of right foot in calorimeter 1,170 c.c., of left 1,085 c.c. The subject was sitting, the feet hanging in the calorimeters.

On May 2, 1911, with an average room temperature of 25.2° C., the flow in the right foot was 3.57 grams, per 100 cubic centimeters per minute, which was only slightly increased (to 3.65 grams) on working the foot, in contrast to the marked increase obtained in the hand on rhythmically closing and unclosing the fist.

May 2, 1911. Right foot put into bath at 3.14 P.M., and into calorimeter at 3.26. The subject sat with his foot hanging in the calorimeter, which contained 5,000 c.c. of water. Left foot and leg not uncovered.

Time.	Temperature of right calorimeter.	Notes.	Time.	Temperature of right calorimeter.	Notes.
3.25½	30.26°	Room temperature 25.1°.	3.37	30.59°	
3.27	30.28°		3.38	30.625°	At 3.38 stopped working foot.
3.28	30.30°		3.39	30.66°	
3.29	30.32°	Room temperature 25.2°.	3.40	30.69°	
3.30	30.35°		3.41	30.71°	
3.31	30.39°		3.42	30.73°	
3.32	30.42°	Room temperature 25.3°.	3.43	30.765°	Room temperature 25.1°.
3.33	30.47°	At 3.33 began to work the foot.	3.44	30.79°	At 3.44 foot out of calorimeter.
3.34	30.49°		3.52	30.71°	
3.35	30.52°		3.53	30.70°	
3.36	30.56°	Room temperature 25.4°.			

Volume of foot in calorimeter 1,220 c.c. Rectal temperature 37.4°. Water equivalent of calorimeter and contents, 6,115 c.c.

Observations on emptying and filling the superficial veins in the hand and foot during such movements show that a greater influence may be expected to be exerted on the flow in the hand. This is confirmed by observations on the foot of C. B., in which the increase of flow during the movements (from 4.73 to 5.32 grams per 100 cubic centimeters of foot per minute), although greater than in the experiment on M. C., is still small in comparison with the increases formerly obtained in the hands.

C. B.—May 2, 1911. Right foot put into bath at 2.19 P.M., and into calorimeter at 2.30$\frac{3}{4}$ P.M. 5,000 c.c. of water in the calorimeter. Pulse (sitting) 72. The subject sat during the blood flow measurements. The left foot and leg were not undressed. The right foot was hanging free in the calorimeter.

Time.	Temperature of right calorimeter.	Notes.	Time.	Temperature of right calorimeter.	Notes.
2.30	29.88°		2.41	30.24°	
2.32	29.91°		2.42	30.275°	At 2.42 stopped working foot.
2.33	29.94°				
2.34	30.00°		2.43	30.31°	Room temperature 26°.
2.35	30.03°	Room temperature 26.3°.	2.44	30.345°	
			2.45	30.39°	
2.36	30.06°		2.46	30.44°	At 2.46 foot out of calorimeter.
2.37	30.10°				
2.38	30.12°	Room temperature 26.3°.	2.56	30.34°	Room temperature 25.7°.
2.38$\frac{1}{6}$		Began to work the foot.	Volume of foot in calorimeter 980 c.c. Rectal temperature 36.9°. Mouth 36.45°. Water equivalent of calorimeter and contents, 5,935 c.c.		
2.39	30.165°				
2.40	30.20°				

To compare the flow in the feet in the sitting and the supine position, which was necessary as a check on the observations in the fever patients, the experiments of March 26, 1913, on M. C., and of March 25, 1913, on J. R. were performed. In the first part of the experiment the subject reclined, with his feet in the calorimeters; then without altering the position of the feet in the least he sat up, the observations being continued without a break. In both experiments the soles of the feet rested throughout the observations on the footrest in the calorimeters. In the same experiments observations were made on the vasomotor reflexes elicited in one foot by immersion of the other in warm or cold water, according to the routine already described for the hand.[6]

M. C.—March 26, 1913. Pulse (sitting) 98. Feet put into bath at 1.42 P.M. At 1.54 P.M. the subject lay down on his back. At 1.56 P.M. feet put into calorimeters. 2,775 c.c. of water in each calorimeter. The calorimeters as finally reduced in capacity were used.

Time.	Temperature of			Notes.	Time.	Temperature of			Notes.
	Calorimeters.		Room.			Calorimeters.		Room.	
	Right.	Left.				Right.	Left.		
1.58	30.87°	30.88°	24.3 °		2.18	31.92°	31.91°	24.3°	
2.00	30.97°	30.93°	24.3°		2.20	31.99°	31.96°		
2.02	31.06°	31.01°		From 2.04 to 2.06 stirring of left calorimeter insufficient.	2.22	32.08°	32.04°	24.6°	
2.04	31.18°	31.14°	24.3°		2.24	32.10°	32.10°		Stirring of right calorimeter insufficient for the last minute.
2.06	31.295°	31.20°		Pulse (lying down) 92.					
2.08	31.43°	31.39°	24.3°						
2.10	31.57°	31.51°							
2.12	31.70°	31.65°	24.1°		2.26	32.18°	32.18°	24.6°	
2.14	31 795°	31.75°		At 2.14 subject sat up and continued sitting for rest of experiment.	2.28	32.23°	32.25°		
					2.30	32.295°	32.31°	24.4°	At 2.30 right foot put in water at 8° C.
2.16	31.87°	31.82°	24.2°		2.32		32.37°		
					2.32½	32.32°			
2.34		32.38°	24.6°	Subject says the left foot feels colder than before.	2.56		32.905°	24.6°	
					2.58		32.99°		
					3.00		33.095°	24.7°	
					3.02		33.22°		
2.36		32.42°	24.6°		3.03				Temperature of right calorimeter 31.80°.
2.38		32.465°	24.6°						
2.40		32.495°							
2.42		32.54°	24.6°						
2.44		32.60°							
2.46		32.68°	24.6°		3.04		33.31°	24.6°	
2.48		32.73°			3.06		33.405°		At 3.06 foot removed from calorimeter.
2.50		32.78°		At 2.50 right foot put in water at 43°.					
2.52		32.80°	24.6°		3.07		33.40°		
2.54		32.86°			3.18		33.17°		Pulse (sitting) 97°.

Cooling of right calorimeter 0.52° in 31½ minutes.

Cooling of left 0.23° in 11 minutes.

Volume of right foot 1,232 c.c., of left 1,195 c.c.

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[6] Stewart, G. N., *Heart, loc cit.*, p. 76.

Hands put into bath at 3.40 P.M. Hands put into calorimeters at 3.52. 3,015 c.c. of water in each calorimeter.

Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Notes.
3.51½	31.10°	31.22°		
3.53	31.10°	31.26°		
3.54	31.18°	31.32°	24.3°	
3.55	31.26°	31.41°		
3.56	31.35°	31.50°		
3.57	31.44°	31.59°		
3.58	31.53°	31.67°	24.3°	
3.59	31.63°	31.76°		
4.00	31.72°	31.81°	24.3°	
4.01	31.795°	31.895°		
4.02	31.87°	31.98°		At 4.02 left hand put in water at 8° C.
4.03	31.91°		24.3°	
4.04	31.98°			
4.05	32.02°		24.4°	
4.06	32.08°			
4.07	32.14°		24.5°	
4.08	32.21°			
4.09	32.27°		24.3°	
4.10	32.31°			

Time.	Temperature of Right calorimeter.	Temperature of Room.	Notes.
4.11	32.37°		
4.12	32.43°	24.4°	
4.13	32.49°		
4.14	32.53°	24.3°	
4.15	32.595°		
4.16	32.67°		At 4.16 left hand put in water at 43° C.
4.17	32.71°	24.4°	
4.18	32.74°		
4.19	32.78°		
4.20	32.83°	24.25°	
4.21	32.88°		
4.22	32.93°	24.35°	
4.23	32.98°		
4.24	33.03°	24.3°	
4.25	33.08°		
4.26	33.125°	24.3°	
4.27	33.22°		At 4.27 hand out of calorimeter. Temperature of left calorimeter 31.40°.
4.53	32.90°		

Cooling of calorimeters, right 0.32° C. in 26 minutes; left 0.58° C. in 51 minutes. Volume of right hand 505 c.c., of left 485 c.c. Rectal temperature 37.1° C. Water equivalent of calorimeters with contents in feet observations, right 3,899, left 3,871. The corresponding numbers for the hand observations are, right 3,499, and left 3,483.

J. R.—March 25, 1913. Feet in bath at 1.44 P.M., and in calorimeters at 1.58 P.M. Pulse (sitting) 85. At 2.01½ P.M. subject lay on his back. 2,775 c.c. of water in each calorimeter, as finally reduced in capacity.

Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Notes.
1.57	30.86°	30.77°		
2.00	30.87°	30.81°		
2.02	30.98°	30.88°		
2.04	31.15°	31.06°	24.8°	
2.06	31.30°	31.19°	25.0°	
2.08	31.48°	31.365°		
2.10	31.66°	31.495°	25.3°	
2.12	31.82°	31.68°		Pulse (lying) 76
2.14	31.95°	31.79°	24.9°	
2.16	32.095°	31.91°	24.7°	Sat up at 2.16 and continued sitting
2.18	32.23°	32.03°	24.6°	

Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Notes.
2.20	32.33°	32.12°	24.6°	
2.22	32.44°	32.20°	24.7°	
2.24	32.58°	32.33°		
2.26	32.72°	32.44°	24.6°	
2.28	32.85°	32.54°	24.6°	
2.30	32.97°	32.65°	24.4°	
2.32	33.02°	32.71°	24.5°	
2.34	33.095°	32.77°		At 2.34¼ right foot put in water at 10° C.
2.36	33.10°	32.81°		
2.38		32.85°		

Time.	Temperature of			Notes.	Time.	Temperature of			Notes
	Calorimeters.		Room.			Calorimeters.		Room.	
	Right.	Left.				Right.	Left.		
2.40		32.885°	24.5°		2.52		33.195°	24.4°	
2.42		32.92°			2.54		33.28°	24.5°	
2.44		32.97°	24.5°	At 2.44 right foot put in water at 43° C.	2.56		33.37°		
2.46		33.025°	24.5°		2.58		33.445°	24.4°	
2.48		33.095°	24.4°		3.00		33.505°	24.4°	Foot removed from calorimeter at 3.00.
2.50		33.13°	24.4°						
					3.03		33.50°		Temperature of right 32.61° C.
					3.26		33.04°		Temperature of right 32.23° C.

Cooling of calorimeters, right 0.87° C. in 50 minutes (0.38° in the last 23 minutes); left 0.46° in 23 minutes. Volume of right foot 1,008 c.c., of left foot 959 c.c.

Hands in bath at 3.30 P.M. At 3.42½ hands in calorimeters. 3,015 c.c. of water in each calorimeter.

Time.	Temperature of			Time.	Temperature of			Notes.
	Calorimeters.		Room.		Calorimeters.		Room.	
	Right.	Left.			Right.	Left.		
3.41	31.22°	31.24°		3.53	31.76°	31.65°	24.8°	Here the cold water was mentioned.
3.43	31.19°	31.26°		3.54	31.795°	31.68°		
3.44	31.22°	31.30°	24.7°	3.55	31.84°	31.695°	24.6°	
3.45	31.295°	31.36°	24.9°	3.56	31.89°	31.73°		
3.46	31.35°	31.40°		3.57	31.95°	31.76°	24.3°	Here the cold water was brought.
3.47	31.40°	31.43°	24.95°	3.58	31.98°	31.78°		
3.48	31.44°	31.465°		3.59	32.02°	31.79°		At 3.59 left hand put in water at 7.8° C.
3.49	31.51°	31.495°		4.00	32.07°		24.4°	
3.50	31.57°	31.53°		4.01	32.08°			
3.51	31.65°	31.58°	24.9°					
3.52	31.71°	31.62°						

Time.	Temperature of		Time.	Temperature of		Time.	Temperature of right calorimeter.	Notes.
	Right calorimeter.	Room.		Right calorimeter.	Room.			
4.02	32.095°	24.4°	4.11	32.36°		4.20	32.82°	Hand removed from calorimeter at 4.20.
4.03	32.11°		4.12	32.38°	24.4°			
4.04	32.13°	24.4°	4.13	32.40°		4.34	32.67°	Temperature of left calorimeter at 4.34 is 31.41°.
4.05	32.155°		4.14	32.44°	24.6°			
4.06	32.195°	24.4°	4.15	32.49°				
4.07	32.225°		4.16	32.56°				
4.08	32.265°		4.17	32.61°	24.4°			
4.09	32.295°	24.3°	4.18	32.66°				
4.10	32.33°		4.19	32.72°	24.5°			

At 4.10 left hand put in water at 43.1°

Cooling of right calorimeter 0.15° in 14 minutes.
Cooling of left calorimeter 0.38° in 35 minutes.
Volume of right hand 393 c.c.
Volume of left hand 376 c.c.
Rectal temperature 37.0° C.

Water equivalent of calorimeters with contents in the feet observations, right 3,731, left 3,694; in the hand observations, right 3,411, left 3,396.

In M. C. the flow in the right foot was 5.11 grams, and in the left 5.23 grams per 100 cubic centimeters of foot per minute lying down, and only 3.96 grams for the right, and 4.17 grams for the left sitting up. In J. R. there was also a reduction in the flow in the sitting position, although less marked than in M. C. (from 7.98 and 7.58 grams for the right and left foot, respectively, to 7.84 and 6.90 grams per 100 cubic centimeters of foot per minute). This is of importance in connection with the fever observations for it permits the assumption that the observed flows were at any rate as large as would have been obtained had the patients been sitting. These observations can therefore be safely compared with all the data obtained on normal persons. It will be noticed that the flows in M. C. in the experiment of March 26, 1913, agree with the results obtained nearly two years previously. This shows that when proper precautions are taken, the range of variation in the observed foot flow in one and the same healthy person is moderate, just as is the case for the hands. Therefore, when great differences, usually in the direction of deficiency, are found in pathological cases it can be assumed with some confidence that they are not due to accidental differences in the external conditions.

The reflex vasomotor effects from one foot to the other are similar to those obtained in the hands, only the constriction elicited by cold seems to be more durable. Thus in M. C. immersion of the right foot in water at 8° C. caused a diminution in the flow in the left foot from 4.17 to 3.12 grams per 100 cubic centimeters per minute for the first ten minutes of the immersion. This gave place rather suddenly, as in the hand, to an increase in the flow (to 5.17 grams per 100 cubic centimeters per minute) for the remaining eight minutes of the immersion. The greater susceptibility to vasoconstriction of the feet than of the hands has already been mentioned in connection with the technique of the measurement since it introduces a possibility of error which must be carefully minimized or excluded, especially in pathological cases, for in not a few clinical conditions this susceptibility seems to be augmented. Where organic local changes are excluded a marked diminution in the foot flow due to vasoconstriction can usually be discriminated from a feeble flow in the feet due to deficient driving power in the circulation, by comparing the flow in the hands under the same conditions. For M. C. this was done in the experiment under discussion. The flow in the hands in the sitting posture came out 14.71 grams per 100 cubic centimeters per minute for the right, and 15.10 grams for the left. Even the greatest foot flow seen in this individual does not approach one half of the hand flow per 100 cubic centimeters of tissue per minute. The average of four experiments on different dates for the right foot in the sitting position is 4.28 grams. The average of nine already published[7] experiments on the hands of M. C. in the sitting position, suitable as regards the range of room temperature and comparable in other respects, is 12.77 grams for the right hand, and 12.29 grams for the left.

In table I, at the end of the following paper,[8] are given the condensed results of nine additional experiments on M. C.'s hands, the average flow in which is 12.95 grams for the right hand, and 12.41 grams for the left. If the observations of May 24, 1911, and November 27, 1911, be excluded, as obviously extreme results due to external temperatures which for the conditions of our experiments may be considered extreme, we get an average of 12.91 grams for the right hand, and 12.61 grams for the left.

In this man, then, the ratio of 1 to 3 holds approximately for the hand and foot flow as determined under our conditions. It is not pretended that the deficiency in the foot flow as compared with the hand flow is in reality exactly as great as this. As already pointed out, the difference between the observed and the actual flow in the foot may be expected to be greater than the corresponding difference for the hand on account of the difference in the dimensions of the two parts. The smaller the foot the closer must the observed come to the actual flow. Yet the error due to this is apparently not great, as is indicated by the comparison of the hand and foot flows in the young boy, N. R. The observations on him were made for the purpose of testing this point. The volume of his feet is no greater than that of M. C.'s hands, in fact somewhat less, and the average thickness of the skin even including that of the soles is probably less. Although the greatest thickness of the boy's foot is probably somewhat greater than the maximum thickness of M. C.'s hand, the dimensions of the two objects do not differ sufficiently to forbid the assumption that the equalization of temperature of the boy's foot and the man's hand with that of the calorimeter would be about equally complete. If then the flow in the adult foot as estimated in this method were much below the actual flow, the measured flow in the boy's foot should approach much nearer to that in his hand than is the case in the adult. That this is not so is shown in the experiment of April 8, 1913.

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[7] Stewart, G. N., *Heart, loc. cit.*, p. 33.

[8] Stewart, G. N., *Jour. Exper. Med., loc. cit.*, table I, p. 385.

N. R., a healthy boy aged 8 years and 9 months. Hebrew. Pulse (sitting) 84. Blood flow measured in feet and hands. Feet in bath at 2.03 P.M., in calorimeters at 2.17½ P.M., and out of calorimeters at 2.55. He sat throughout the examination. 3,015 c.c. of water in each foot calorimeter, as finally reduced in capacity. An additional footrest was used to bring the flange of the calorimeter to the same level on the ankle as in the observations with adults. His legs were loosely wrapped up with towels down to the calorimeters.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.13	30.87°	30.89°	23.5°	2.39	30.92°	30.85°	23.95°
2.19	30.80°	30.80°	24.2°	2.41	30.93°	30.86°	23.95
2.21	30.80°	30.80°	24.3°	2.43	30.96°	30.87°	24.0°
2.23	30.795°	30.795°	24.3°	2.45	30.965°	30.875°	24.0°
2.25	30.805°	30.80°	24.3°	2.47	30.99°	30.88°	24.0°
2.27	30.82°	30.805°		2.49	31.02°	30.91°	24.0°
2.29	30.825°	30.81°	24.1°	2.51	31.04°	30.915°	24.0°
2.31	30.85°	30.81°	24.0°	2.53	31.05°	30.92°	24.1°
2.33	30.87°	30.82°	24.0°	2.55	31.07°	30.925°	
2.35	30.89°	30.82°	24.0°	2.57	31.08°	30.89°	
2.37	30.90°	30.825°	23.95°	3.34	30.58°	30.39°	

Cooling of calorimeters in 37 minutes, right 0.50°, left 0.50°. Volume of right foot 491 c.c., of left foot 480 c.c. Water equivalent of calorimeters with contents, right 3,593, left 3,585.

Hands in bath at 3.26 P.M., in calorimeters at 3.37½ P.M., and out of calorimeters at 3.58. 3,115 c.c. of water in each hand calorimeter.

Time.	Temperature of Calorimeters.		Temperature of Room.	Time.	Temperature of Calorimeters.		Temperature of Room.
	Right.	Left.			Right.	Left.	
3.37	30.82°	30.98°		3.49	30.94°	31.105°	
3.39	30.82°	30.96°	23.9°	3.50	30.96°	31.11°	24.0°
3.40	30.83°	30.98°	23.9°	3.51	30.965°	31.11°	
3.41	30.835°	30.99°		3.52	30.975°	31.125°	24.0°
3.42	30.84°	30.995°	23.85°	3.53	30.99°	31.135°	
3.43	30.845°	31.00°		3.54	31.00°	31.145°	24.1°
3.44	30.85°	31.015°	23.9°	3.55	31.00°	31.15°	
3.45	30.88°	31.04°		3.56	31.02°	31.175°	
3.46	30.90°	31.06°	23.95°	3.57	31.04°	31.195°	24.1°
3.47	30.915°	31.095°		3.58	31.095°[9]	31.19°[9]	
3.48	30.935°	31.10°	24.0°	4.14	30.95°[9]	31.00°[9]	

Pulse (sitting) 80. Rectal temperature 37.2°.

Cooling of calorimeters in 16 minutes, right 0.145°, left 0.19°. Volume of right hand 206 c.c., of left hand 180 c.c. Second observation on hand volumes, right hand 200 c.c., left 182 c.c. Average for right 203 c.c., for left 181 c.c. Water equivalent of hand calorimeters with contents, right 3,357, left 3,340.

In this experiment the blood flow in the feet for the last eighteen minutes of the immersion in calorimeters was 3.37 grams per 100 cubic centimeters of foot per minute for the right foot, and 2.86 grams for the left. For the hands for the last 15 minutes in the calorimeters the flow was 8.22 grams per 100 cubic centimeters per minute for the right hand, and 8.95 grams for the left. Considering only the last ten minutes in the calorimeters, the flow comes out 8.08 grams per 100 cubic centimeters per minute for the right hand, and 7.75 grams for the left. In round numbers the hand flow (average of the two hands) is 8 grams per 100 cubic centimeters of tissue, and the foot flow (average of the two feet) 3 grams per 100 cubic centimeters of tissue, practically the same ratio as in M. C. The smaller calculated flow in the foot than in the hand of the adult is therefore not due to more complete equalization of the temperature of the hand with that of the water than is the case for the foot.

In C. B. in the experiment of May 2, 1911, the flow in the right foot was 4.73 grams per 100 cubic centimeters per minute, with room temperature a little over 26° C., whereas the highest flow observed in his hands on an extremely hot day, with room temperature 28.9°, was 12.54 grams for the right and 13.34 grams for the left (May 22, 1911), and the average of all hand observations on this man works out at 8.4 grams per 100 cubic centimeters per minute. The ratio of the volume of C. B.'s foot to M. C.'s is about 1 to 1.25.

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[9] These readings were all verified.

In the experiment of March 25, 1913, on J. R., comparison is complicated by the fact that the left hand has a much smaller flow than the right (12.38 grams per 100 cubic centimeters per minute for the right, 8.82 grams for the left). A difference as great as this is rare in normal persons. In fact, in those I have examined there is no other instance, although in clinical cases with unilateral anatomical differences and even without such in certain neurological conditions, still greater differences may be found. Where a difference of any magnitude is temporary, that is to say, where it is obtained one day and not the next, or the next week, it cannot be far wrong to interpret it as due to such an accidental vasomotor difference as is familiar in other parts; for example, when one ear is hot and red and the other cold and pale. In J. R., however, the same difference between the hands was found on March 22, 1913, 10.08 grams per 100 cubic centimeters per minute for the right hand, and 7.25 grams for the left, with room temperature 24.0° C. The ratio between the flows in the left and right hands is the same (1 to 1.39) as on March 25, when it was 1 to 1.40.

In the absence of further examination, which will be made later, all that can be said is that this indicates some permanent condition on which the inequality of the flow in the two hands depends. The young man states that he feels well, but he bleeds easily. A week before the examination of March 22 he lost half a glass of blood by bleeding from the nose. A small cut on the finger bled for fifteen minutes a few days after. He says that cuts always bleed a long time. He states that a brother and a sister bleed easily and the bleeding is difficult to stop. Some of his cousins also have this peculiarity. The slow pulse rate, not responding to change of posture, on March 22, and the much more rapid rate on March 25 are also peculiar features, and it is possible that this case should not be considered entirely a normal one. At any rate, for our purpose it will be safest to neglect the left hand. The ratio between the flows in the right foot and right hand in the sitting posture then comes out approximately 1 to 1.6. The ratio of the combined volume of his feet to the combined volume of the feet of M. C. is 1 to 1.28.

J. R.—March 22, 1913. Hands in bath at 11.55 A.M., in calorimeters at 12.06¾ P.M. 3,015 c.c. of water in each calorimeter. Pulse (sitting) 52, counted for a minute at the end of the examination. Just before the examination of the hands the rate was 52 and 51 for two successive minutes in the supine position.

Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Notes.	Time.	Temperature of Calorimeters. Right.	Temperature of Calorimeters. Left.	Temperature of Room.	Notes.
12.06	30.69°	30.75°	.		12.16	30.91°	30.89°	24.0°	
12.08	30.59°	30.71°			12.17	30.94°	30.91°		
12.09	30.60°	30.715°	22.7°	Radiator turned on.	12.18	30.99°	30.93°	24.1°	
12.10	30.605°	30.72°	22.9°		12.19	31.04°	30.97°	24.2°	
12.11	30.65°	30.745°	22.9°		12.20	31.10°	30.995°		
12.12	30.695°	30.77°	22.95°		12.21	31.125°	31.00°	24.3°	
12.13	30.73°	30.78°			12.22	31.18°	31.03°		At 12.22 he saw the cold water.
12.14	30.79°	30.80°	23.8°		12.23	31.20°	31.04°		At 12.23 left hand in water at 8° C.
12.15	30.83°	30.83°	23.7°		12.24	31.235°			
12.25	31.25°		24.3°		12.38	31.425°		23.95°	
12.26	31.26°		24.3°		12.39	31.46°			
12.27	31.27°				12.40	31.49°			
12.28	31.28°		24.2°		12.41	31.52°		23.9°	
12.29	31.295°				12.42	31.58°			
12.30	31.31°				12.43	31.62°		23.85°	
12.31	31.325°		24.0°		12.44	31.68°			
12.32	31.345°				12.45	31.75°		24.0°	
12.33	31.38°		24.0°		12.46	31.795°			
12.34	31.39°				12.47	31.84°		24.1°	
12.35	31.40°				12.48	31.92°			Hand out of calorimeter at 12.48.
12.36	31.41°		23.95°	At 12.36 left hand in water at 43.2°.					
12.37	31.42°				1.01	31.80°	30.64°		

Cooling of calorimeters, right 0.12° C. in 13 minutes, left 0.40° C. in 38 minutes. Volume of right hand 397 c.c., of left hand 354 c.c. Water equivalent of calorimeters with contents, right 3,412, left 3,378. Rectal temperature 36.5° C.

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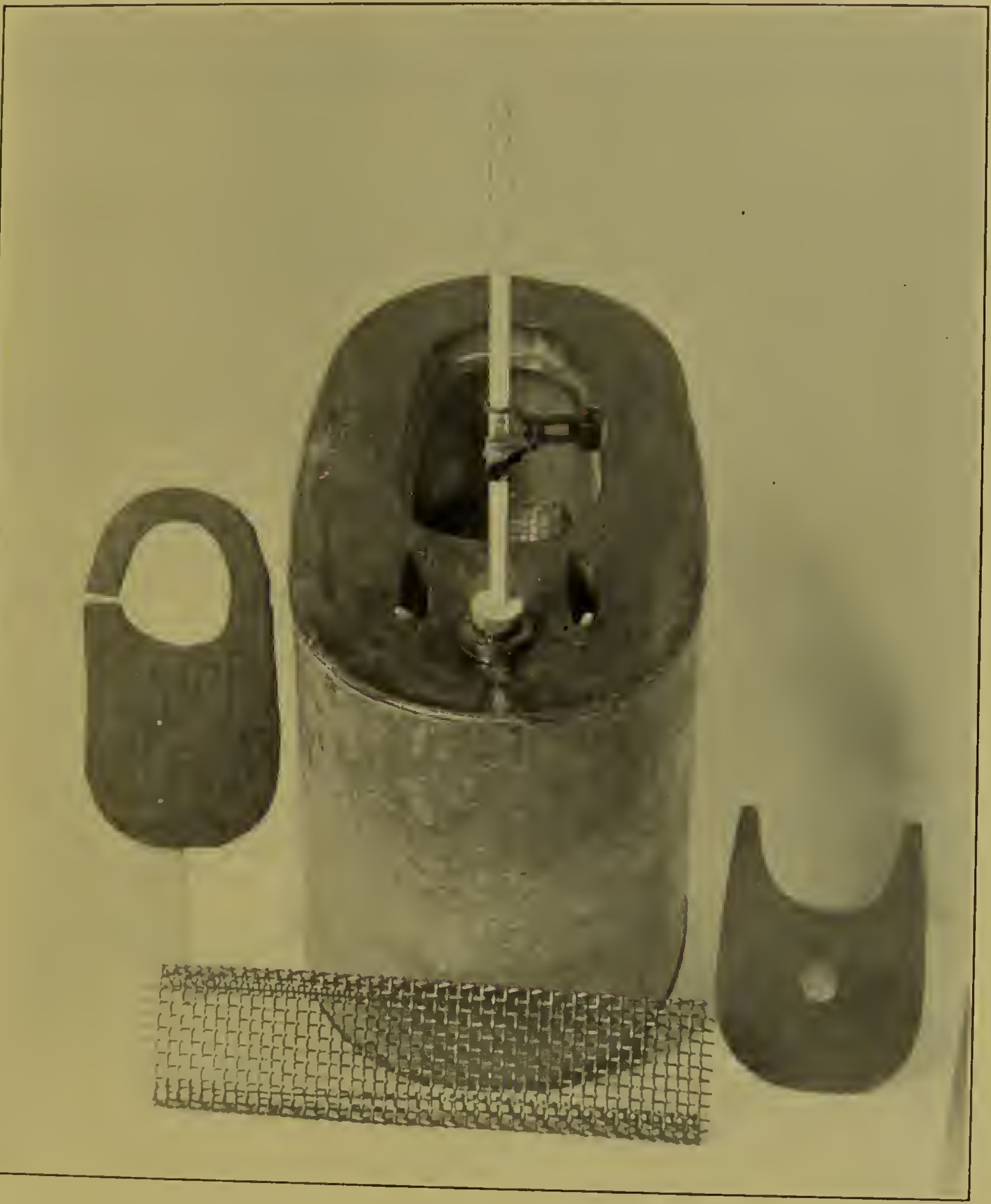

FIG. 1.

(Stewart: Studies on the Circulation in Man.

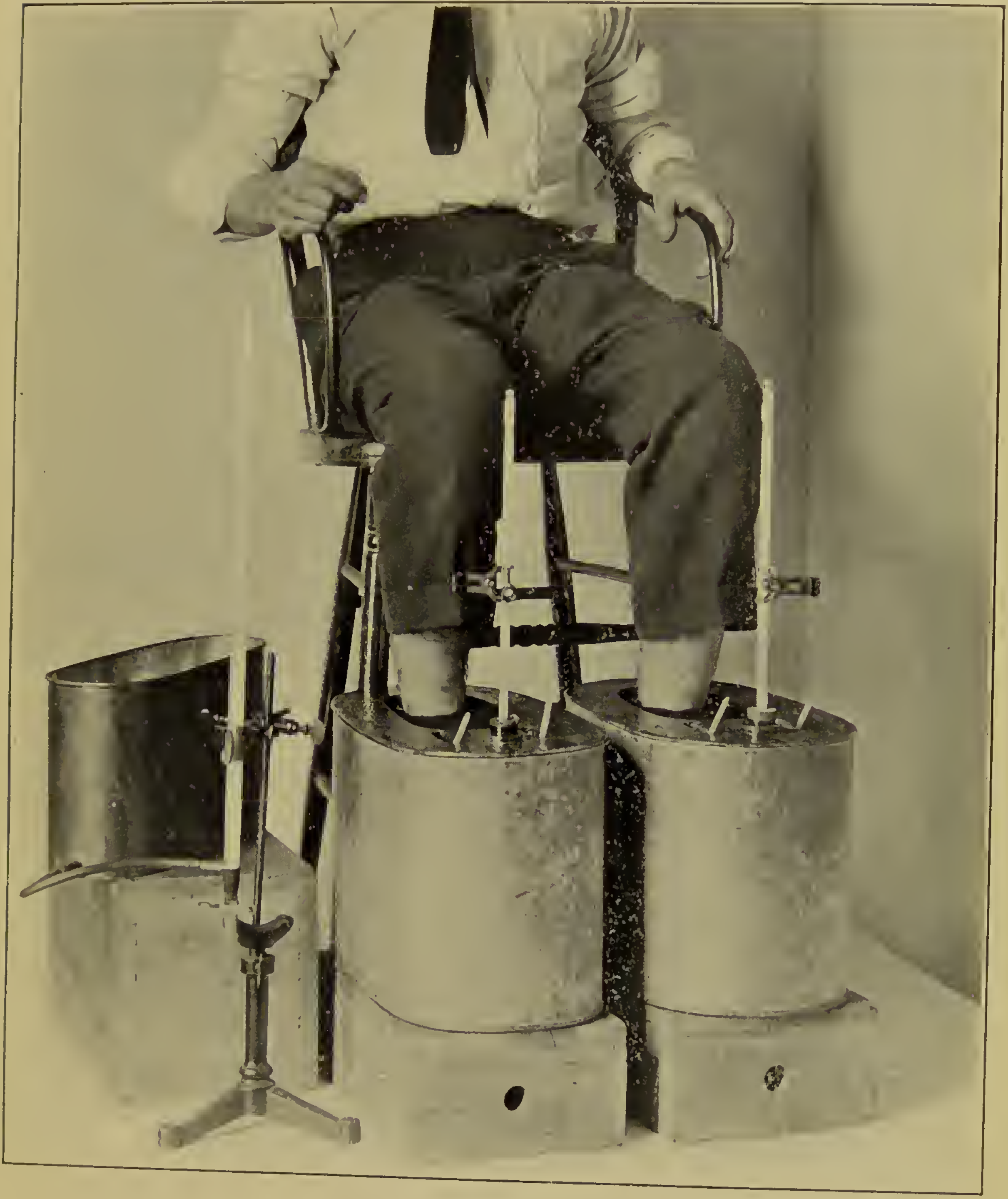

FIG. 2.

(Stewart: Studies on the Circulation in Man.)

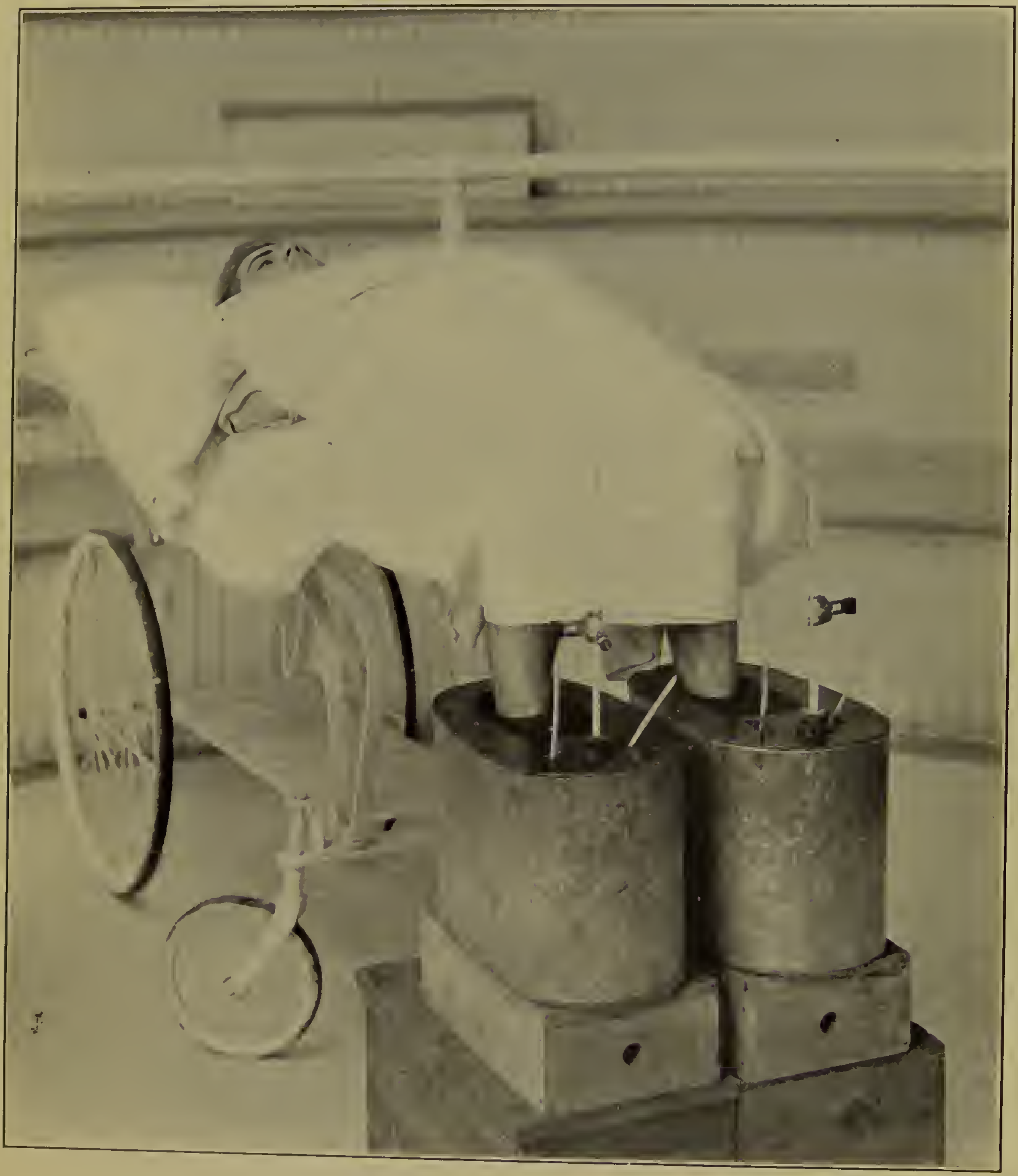

FIG. 3.

(Stewart: Studies on the Circulation in Man.

It will, therefore, probably not be far wrong to assume that in normal adults the ratio between the foot flow and the hand flow as estimated in this way will not pass much in either direction beyond the limits 1 to 3 and 1 to 2. Where we encounter foot flows which, in the absence of known anatomical causes, obliterative arteritis for example, are much below one third of the hand-flow in the same person, we shall usually not be wrong in concluding that the peripheral resistance in the path through the feet is increased in proportion to that of the path through the hand, and that in general the increase is due to vasomotor influence.

CONCLUSIONS.

1. The blood flow in the feet is smaller per unit of volume of the part than in the hand, the ratio of foot flow to hand flow per 100 cubic centimeters of the part usually lying in normal persons between 1 to 3 and 1 to 2.
2. In the supine position, with the legs hanging down, the flow in the feet seems to be somewhat greater than in the sitting position.

EXPLANATION OF PLATES.

Plate 22.

Fig. 1. Foot calorimeter. For description see text (p. 354).

Plate 23.

Fig. 2. Arrangement for the measurement of foot flow with the patient in sitting position. At the left is shown the arrangement for measuring the volume of the feet. The legs should be more completely covered.

Plate 24.

Fig. 3. Arrangement for measuring the foot flow in a patient not well enough to sit up. The legs should be more completely covered than is indicated in the figure.

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STUDIES ON THE CIRCULATION IN MAN.

VIII. The Blood Flow in the Feet with Special Reference to Fever.*

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In spite of much discussion we possess but little exact knowledge of the changes in the cutaneous circulation in fever, which constitute an essential, probably the chief, factor in the derangement of the temperature-regulating mechanism. I have endeavored to make a small contribution to our data by measuring approximately the blood flow in the feet in a number of cases of typhoid fever and in one case of pneumonia. Of one of the cases of typhoid four examinations were made in the course of a month. In a second case a similar program was planned but had to be modified on account of hemorrhage, and only two examinations were carried out. These, however, happened to be at the most interesting stages in the course of the fever. For comparison three cases at different stages in convalescence were investigated, each on one occasion. In the pneumonia case two examinations were secured, the last one four days before the death of the patient. The first of the typhoid patients was far enough advanced in convalescence to permit him to sit up in a chair for the examination of the hands.

F. D.—A sailor, aged 26 years, height 5 feet 9½ inches, was admitted to the City Hospital on September 5, 1912, suffering from typhoid fever. About a month before he fell into the Cuyahoga River and swallowed water. The drinking water on the lake boats on which he works is, according to him, far from being beyond suspicion, as it is taken from the lake. His maximum temperatures were as follows:

September	5,	104.0° F.	September	10,	104.0° F.
September	11,	103.4° F.	September	12,	102.4° F.
September	15,	100.0° F.	September	17,	98.6° F.

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* Received for publication, April 30, 1913.

Only one examination of the blood flow was obtained, and that was when he was so far advanced in convalescence that he walked into the room. The foot flow was measured, as in the other cases, while he lay on his back on the movable bed.

October 1, 1912. Feet put into bath at 1.21 P.M., and into calorimeters at 1.38½ P.M. 3,740 c.c. of water in each calorimeter. Pulse (lying on back) 81.

Time.	Temperature of		
	Calorimeters.		Room.
	Right.	Left.	
1.37	31.19°	31.16°	
1.42	31.02°	30.95°	22.1°
1.44	30.99°	30.94°	
1.46	30.97°	30.92°	21.8°
1.48	30.945°	30.89°	22.1°
1.50	30.935°	30.87°	
1.52	30.92°	30.86°	22.3°
1.54	30.91°	30.845°	
1.56	30.90°	30.835°	22.5°
1.58	30.895°	30.815°	22.45°
2.00	30.89°	30.80°	
2.02	30.88°	30.79°	22.45°
2.04	30.875°	30.78°	22.45°
2.06	30.87°	30.77°	
2.08	30.82°	30.73°	
2.18	30.66°	30.565°	22.45°

Cooling in 10 minutes of right calorimeter 0.16° C., of left 0.165°. Volume of right foot 1,135 c.c., of left 1,117 c.c. Feet out of calorimeters at 2.06½.

Immediately afterward the flow in the hands was measured. Hands put into bath at 2.32 P.M., and into calorimeters at 2.42½ P.M. 3,015 c.c. of water in each calorimeter. Pulse (sitting) 90. Blood pressure, left arm, systolic 106 (palpation), 107 (stethoscope); 82 (sound gone). Another observation, systolic 109, 85 (sound gone).

Time.	Temperature of			Notes.
	Calorimeters.		Room.	
	Right.	Left.		
2.41	31.71°	31.69°	22.9°	
2.43	31.70°	31.70°		
2.44	31.76°	31.74°	23.2°	
2.45	31.80°	31.77°		
2.46	31.84°	31.81°	23.1°	
2.47	31.88°	31.85°		
2.48	31.91°	31.88°		
2.49	31.935°	31.905°		
2.50	31.97°	31.94°		Room temperature 22.8°.
2.51	31.99°	31.96°		
2.52	32.02°	31.985°		Room temperature 22.8°.
2.53	32.06°	32.02°		Hands out of calorimeters at 2.53.
3.07	31.84°	31.81°		

Cooling in 14 minutes of right calorimeter 0.22°, of left 0.21°. Volume of right hand 425 c.c,. of left 423 c.c. Patient is ambidextrous. Rectal temperature, 37.2°. Water equivalent of right calorimeter and contents 3,435; of left and contents 3,434.

Here the hand flow lies within the normal range, being 9.16 grams per 100 cubic centimeters per minute for the right hand, and 8.63 grams for the left, with room temperature 23° C. The foot flow is much below the normal (0.98 grams per 100 cubic centimeters per minute for the right, and 0.85 grams for the left). The ratio of the combined foot flows to the combined hand flows (1 to 9.7) is much too small and indicates clearly an abnormal sensitiveness of the feet to vasoconstriction, the exciting cause being probably the necessary exposure of the feet to the air and water. We shall see that there is evidence in the foot flows of abnormally great cutaneous vasoconstriction in all the typhoid cases examined, and at all stages of the fever which happened to coincide with an examination. This tendency to vasoconstriction seems to be carried into convalescence.

In the case of J. McD., who was still further advanced in convalesence than F. D., the prolonged reflex vasoconstriction, not followed by any vasodilatation in the left hand when the right was immersed in warm water, might be interpreted in the same way, as also the marked inferiority of the flow in the right hand as compared with the left. Such differences between the two hands in the absence of any known anatomical cause are apt to be observed in persons who exhibit other evidences of nervous, including vasomotor, instability.

J. McD.—A laborer, aged 26 years, was admitted to the City Hospital on April 11, 1912, suffering from typhoid fever. The maximum temperature reached was 105.6° F. on April 12 and April 13. The opportunity to examine his blood flow was not offered until he was convalescent. Temperature at 4 A.M. on May 16, 98.5° F. He is emaciated and his appetite is ravenous.

The blood flow in the hands was examined on May 16, 1912. Hands in bath at 1.47 P.M., and in calorimeters at 1.56½ P.M. 3,015 c.c. of water in each calorimeter. Mouth temperature 36.7° C. Pulse (sitting) 80.

Time.	Temperature of calorimeters.		Notes.
	Right.	Left.	
1.56	30.92°	31.11°	
1.58	30.94°	31.12°	Room temperature 22.6°
1.59	30.97°	31.15°	
2.00	31.00°	31.20°	
2.01	31.04°	31.23°	Room temperature 23.1°
2.02	31.08°	31.27°	
2.03	31.10°	31.31°	
2.04	31.14°	31.35°	
2.05	31.19°	31.41°	Room temperature 23.2°
2.06	31.22°	31.455°	
2.07	31.28°	31.52°	Room temperature 23.6°.
2.08	31.315°	31.555°	
2.09	31.37°	31.625°	Ears red.
2.10	31.405°	31.66°	Room temperature 23.2°.
2.11	31.44°	31.72°	
2.12	31.48°	31.75°	
2.13	31.52°	31.81°	
2.14	31.56°	31.84°	Room temperaature 23.1°.
2.15	31.59°	31.90°	
2.16	31.62°	31.93°	At 2.16 right hand put in water at 8°. Room temperature 23.0°.

Time.	Temperature of calorimeters.		Notes.
	Right.	Left.	
2.17		31.945°	
2.18		31.96°	Room temperature 23.2°
2.19		31.99°	
2.20		32.03°	
2.21		32.055°	
2.22		32.08°	
2.23		32.12°	Room temperature 23.2°
2.24		32.155°	Right hand in the cold water is redder than is usually the case
2.25		32.20°	
2.26		32.23°	Right hand put in water at 42.9°
2.27		32.24°	Room temperature 23.0°
2.28		32.26°	
2.29		32.305°	Room temperaature 23.0°.
2.30		32.33°	
2.31		32.35°	Room temperature 23.1°.
2.32		32.38°	
2.33		32.41°	
2.34		32.425°	Room temperature 23.6°.
2.35		32.435°	
2.36		32.455°	Hand out of calorimeter at 2.36. Room temperature 23.7°.
2.44		32.35°	Temperature of right calorimeter 31.29°.

Cooling of right calorimeter in 28 minutes, 0.33°; of left in 8 minutes, 0.105°.

Volume of right hand 511 c.c., of left hand 505 c.c. His hands are large although they have lost a considerable proportion of the soft tissues.

In this experiment the flow for a period of eighteen minutes before the vasomotor reaction was tested was 6.95 grams per 100 cubic centimeters per minute for the right hand and 8.42 grams for the left. During the first five minutes of immersion of the right hand in cold water the flow in the left was reduced to 6.10 grams per 100 cubic centimeters per minute and rose again to 8.04 grams for the next five minutes of immersion. When the right hand was put into warm water the flow in the right fell to 6.25 grams per 100 cubic centimeters per minute for the whole period of immersion (ten minutes).

Hyperexcitability of the vasoconstrictor mechanisms of the periphery is most naturally interpreted as a defensive reaction of the organism by which an increased supply of blood is afforded for those internal organs which bear the brunt of the infection. The fact that the blood pressure is low and the pulse dicrotic in spite of the constriction of the vessels of the periphery, indicates that other vascular paths, especially the splanchnic area, are more widely opened than usual. The fever, the rise of temperature of the internal parts and of the blood, may be considered as, in the main, a secondary and inevitable, and perhaps in itself an unimportant consequence of a sustained cutaneous vasoconstriction. When the temperature has risen to a certain height a balance between heat production and heat loss is necessarily again reached in spite of the vasoconstriction. Indeed, were the circulation in the skin entirely stopped it is clear that such a balance must also be eventually reached by augmentation of the flow of heat by conduction from the deeper parts.

It must be remembered that with a normal flow through the skin in fever the amount of heat given off would be greater than normal on account of the higher temperature of the blood. Table I illustrates this point. Thus while the amount of heat given off per 100 cubic centimeters of foot per minute in all the fever cases does not rise beyond the range for the normal persons, the amount of heat given off per gram of blood passing through the foot is much greater in fever than with normal body temperature. And it is precisely when the flow of blood is small and the rectal temperature high that the heat loss per gram of blood is greatest. Thus in J. B. on October 16, 1912, with rectal temperature 40.2° C., and in M. V. on October 8, 1912, with rectal temperature 40.5° C., over eight small (gram) calories per gram of blood are given off to the calorimeters, whereas the corresponding number for the normal persons is always below six for the average of the two feet. A glance at table II will show that the difference does not depend upon variations in the calorimeter temperatures in the different experiments. It is essential to point this out as it is obvious that it is inherent in the method that the lower the calorimeter temperature the greater must be the heat loss per gram of blood passing through the part. The slight differences in the heat given off by the two hands or by the two feet in one and the same experiment depend upon differences in the calorimeter temperatures.

If the cutaneous vasoconstriction is in the interests of an increase in the blood flow to the organs on which the stress of the infection falls, it is plain that if the increased temperature is to be combatted by direct measures the most rational procedure is to hasten the loss of heat without dilatation of the skin vessels, or still better while their constriction is even increased. This indication is admirably met by the cold bath treatment. On the other hand, the use of antipyretics which act by causing cutaneous vasodilatation would seem to be unphysiological since in diminishing the temperature they cause the withdrawal of blood from the seats of infection.

F. S.—A laborer, aged 28 years, was admitted to the City Hospital on September 16, 1912, suffering from typhoid fever. He became ill a week before admission, had two chills, and vomited twice. Pulse dicrotic, low tension. The maximum temperatures were as follows:

September 17,	104.4° F.	September 19,	104.0° F.
September 20,	104.0° F.	September 21,	104.0° F.
September 24,	103.0° F.	September 26,	102.0° F.
October 1,	100.0° F.		

It was only possible to examine the blood flow once and that was during convalescence.

The blood flow in the feet was examined on October 2, 1912. Pulse (reclining on back) 72. Feet in bath at 2.43 P.M., in calorimeters at 2.56½ P.M. 3,740 c.c. of water in each calorimeter. Blood pressure, right arm, systolic 106 (palpation), 104 (stethoscope); 77 (sudden diminution of sound), 58½ (disappearance of sound). Rectal temperature 37.9° C.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.55	31.77°	31.69°		3.16	31.795°	31.59°	24.15°
2.59	31.71°	31.55°	23.9°	3.18	31.80°	31.60°	24.2°
3.01	31.71°	31.55°	23.9°	3.20	31.805°	31.61°	24.15°
3.03	31.725°	31.565°	23.95°	3.22	31.81°	31.625°	24.1°
3.05	31.73°	31.57°	24.1°	3.24	31.825°	31.63°	
3.07	31.75°	31.575°		3.26	31.795°	31.595°	
3.09	31.77°	31.585°	24.15°	3.44	31.52°	31.325°	
3.11	31.78°	31.59°	24.2°				
3.13	31.78°	31.585°	24.2°				

Cooling of right calorimeter 0.275° in 18 minutes, of left 0.27°. Volume of right foot 1,295 c.c., of left foot 1,258 c.c. Feet out of calorimeters at 3.24½.

The patient was examined about a fortnight after admission and ten days after the fastigium. The flow was distinctly below normal, in the right foot 1.47 grams per 100 cubic centimeters per minute; in the left 1.39 grams, the room temperature being 24.1° C.

M. V.—A laborer, aged 29 years, height about 6 feet, was admitted to the City Hospital on October 7, 1912, eight days after he became ill with typhoid. He was quite ill on admission. Rose spots. Maximum temperature October 7 at 10 P.M. 105.6° F. Temperature October 8 at 5 A.M. 103.4° F. He had a full bath on October 7 and another on October 8 about 1 P.M.

First Examination of Blood Flow.—October 8, 1912. Feet in bath at 3.01 P.M., and in calorimeters at 3.18 P.M. 3,740 c.c. of water in each calorimeter. Pulse (lying on back) 108. Blood pressure, right arm, systolic 118, 89 (sound entirely gone). Rectal temperature 40.5° C.

Time.	Temperature of		
	Calorimeters.		Room.
	Right.	Left.	
3.13	31.06°	30.93°	22.3°
3.20	30.89°	30.74°	22.4°
3.22	30.86°	30.72°	21.8°
3.24	30.84°	30.71°	21.9°
3.26	30.835°	30.74°	22.1°
3.28	30.86°	30.755°	22.2°
3.30	30.88°	30.79°	22.15°
3.32	30.92°	30.85°	22.15°
3.34	30.95°	30.88°	22.1°
3.36	31.01°	30.91°	22.15°
3.38	31.03°	30.945°	22.2°
3.40	31.095°	30.98°	
3.42	31.04°	30.95°	
3.59	30.79°	30.695°	

Cooling of right calorimeter 0.25° in 17 minutes, of left 0.255°. Volume of right foot 1,322 c.c., of left, 1,294 c.c. Feet out of calorimeters at 3.40.

Second Examination.—November 5, 1912. The patient says that he is now feeling well. The maximum and minimum temperatures were as follows:

October 9, 105.0° and 102.6° F.
October 10, 104.8° and 103.0° F.
October 11, 104.0° and 102.0° F.
October 14, 105.0° and 101.0° F.
October 17, 104.6° and 102.0° F.

On October 17 he had a hemorrhage from the bowels, and on October 18 a hemorrhage from one ear. On October 30 the maximum temperature was still 104.0° F., the minimum 100.0°. From that date the temperature steadily diminished to 101.4° (maximum) and 98.4° (minimum) on November 4.

Feet in bath at 2.43 P.M. (lying on back on the ambulance). Pulse 80. Feet in calorimeters at 2.54 P.M. 2,775 c.c. of water in each calorimeter. The capacity of the calorimeters had been reduced since the last examination. The volumes of the feet are therefore not strictly comparable in the two experiments. Rectal temperature 37.95° C. Blood pressure, right arm, systolic 107, 62 (sound gone). Another observation, systolic 108, 82 (abrupt diminution in sound); 65 (sound gone).

Time.	Temperature of		
	Calorimeters.		Room.
	Right.	Left.	
2.52	30.68°	30.76°	
2.56	30.62°	30.70°	23.1°
2.58	30.675°	30.77°	22.9°
3.00	30.68°	30.79°	22.9°
3.02	30.695°	30.80°	22.9°
3.04	30.71°	30.83°	22.8°
3.06	30.71°	30.83°	22.8°
3.08	30.72°	30.855°	22.9°
3.10	30.725°	30.865°	22.9°
3.12	30.73°	30.875°	
3.14	30.68°	30.85°	
3.30	30.40°	30.58°	23.0°

Cooling in 16 minutes of right calorimeter 0.28°, of left 0.27°. Volume of right foot in calorimeter 1,109 c.c.
Volume of left foot in calorimeter 1,100 c.c.

M. V. was examined for the first time the day following his admission to the hospital. His rectal temperature was 40.5° C. (104.9° F.), although he had had a full bath two hours before the examination. The flow was only 1.54 grams per 100 cubic centimeters of foot per minute for the right foot, and 1.50 grams for the left, with room temperature 22.2° C. On account of the hemorrhage mentioned in the protocol nine days after the first examination, it was not considered justifiable to carry out the original program, since, although the examination caused apparently very little disturbance to the patient, absolute rest was obviously enjoined in this case. Accordingly an interval of exactly four weeks elapsed between the first and the second examination of the blood flow. His rectal temperature at the second examination was 37.95° C. (100.3° F.). The foot flow was somewhat smaller than at the first examination (1.24 grams per 100 cubic centimeters per minute for the right, and 1.40 grams for the left, with room temperature 22.9°). Of course the amount of heat given off per minute to the calorimeter was much greater at the first examination than at the second on account of the higher blood temperature. This renders it necessary to state that it has not hitherto been feasible to determine by actual experiment in a fever case the relation between the rectal temperature and the temperature of the arterial blood at the ankle under the average conditions of our blood flow observations. It has been assumed in the calculations that the difference is 0.6° C., the same as for a normal person. It is, of course, possible that in fever the temperature of the blood as it passes from the heart to the wrist or ankle falls more than in health, since the excess of temperature of the skin over that of the surroundings is greater. Yet the arterial blood moves so rapidly and the large arteries are so well protected that it can scarcely be supposed that any considerable difference exists. It must be taken into account also that in the observations the limbs were covered as far as possible down to the calorimeters. It may therefore be confidently assumed that the calculations are not vitiated in any important degree by the want of direct experimental control of this factor.

The greatest number of observations were obtained on J. B.

J. B.—A laborer, aged 24 years, was admitted to the City Hospital on September 23, 1912, suffering from typhoid fever. He had been ill for three weeks with alternate attacks of diarrhea and constipation, and malaise. He was quite ill when brought to the hospital and was delirious on September 25. Spleen enlarged and tender. Pulse, low tension, small volume, and dicrotic. Maximum temperature September 25, 105.8° F.; temperature October 1 at 4 P.M. 104.0°; October 2 at noon 101.6°.

First Examination of Blood Flow.—October 2, 1912. The patient seemed quite ill when brought in on the ambulance and lay on his back perfectly still throughout the examination. Feet in bath at 1.18 P.M., and in calorimeters at 1.34½ P.M. His feet are small. 3,740 c.c. of water in each calorimeter. Pulse 108. Blood pressure, right arm, systolic 102 (palpation), 100 (stethoscope); 78 (sound gone).

Time.	Temperature of			Time.	Temperature of calorimeters.		Notes.
	Calorimeters.		Room.		Right.	Left.	
	Right.	Left.					
1.32	31.03°	31.08°		1.51	31.32°	31.50°	Room temperature 24.35°.
1.37	30.93°	31.01°	24.3°	1.53	31.375°	31.58°	
1.39	30.96°	31.08°	24.4°	1.55	31.45°	31.67°	Feet out of calorimeters at 1.55.
1.41	31.00°	31.14°	24.4°				
1.43	31.06°	31.20°	24.3°	1.57	31.425°	31.65°	Room temperature 24.3°.
1.45	31.12°	31.28°		2.17	31.12°	31.35°	
1.47	31.19°	31.35°	24.4°				
1.49	31.26°	31.415°					

Cooling of right calorimeter in 20 minutes, 0.305°, of left 0.30°.
Volume of right foot 927 c.c., of left 945 c.c.
Rectal temperature 39.35°.

Second Examination.—October 8, 1912. The maximum temperature has continued high since the last examination. Temperature at 2.30 P.M. on October 7, 105.4° F., at 10 P.M. 105.0° F.; October 8 at 8 A.M. 101.0° F. The patient has had an ice cap on his head, and this was on during the examination. Feet in bath at 1.49 P.M., and in calorimeters at 2.04½ P.M. 3,740 c.c. of water in each calorimeter. Pulse 104. Blood pressure, right arm, systolic 109 (stethoscope and palpation); diastolic 80 (sound abruptly diminished), 65 (sound gone entirely).

Time.	Temperature of			Time.	Temperature of			Notes.
	Calorimeters.		Room.		Calorimeters.		Room.	
	Right.	Left.			Right.	Left.		
2.02	30.74°	30.72°		2.20	30.295°	30.23°	22.4°	
2.06	30.59°	30.50°		2.22	30.26°	30.19°	22.4°	
2.08	30.52°	30.45°		2.24	30.23°	30.17°	22.1°	
2.10	30.47°	30.395°	21.4°	2.26	30.20°	30.145°		Feet out of calorimeters at 2.26.
2.12	30.43°	30.36°	21.6°					
2.14	30.39°	30.33°	21.9°					
2.16	30.36°	30.28°	22.1°	2.28	30.17°	30.10°		
2.18	30.32°	30.25°	22.2°	2.45	29.89°	29.82°	22.2°	

Cooling of right calorimeter 0.28° in 17 minutes, and of left 0.28°.
Volume of right foot 924 c.c., of left 900 c.c.
Rectal temperature at 3 P. M. 39.45° C.

The feet were somewhat blue when taken out of calorimeters.

Third Examination.—October 16, 1912. The patient still has the ice cap on. Temperature at noon on October 9, 99.8° F., at 4 P.M. 104.4°; October 10 at noon 101.4° F., at 8 P.M. 103.8°; October 11 at 6 P.M. 104.0° F. Since this time it has gradually fallen. On October 16 at 8 A.M. it was 99.4°, and at noon 101.0°. He says that he has no appetite. Blood pressure, right arm, systolic 104 (palpation), 105½ (stethoscope); 66 (sound gone). Pulse 106. Feet in bath at 1.54 P.M., in calorimeters at 2.08 P.M. 3,740 c.c. of water in each calorimeter.

Time.	Temperature of			Time.	Temperature of		
	Calorimeters.		Room.		Calorimeters.		Room.
	Right.	Left.			Right.	Left.	
2.05	31.29°	31.24°		2.32	30.62°	30.67°	23.1°
2.10	31.03°	31.04°	23.1°	2.34	30.60°	30.665°	22.9°
2.12	30.95°	31.01°	22.9°	2.36	30.58°	30.65°	
2.14	30.91°	30.95°	22.8°	2.38	30.55°	30.61°	23.1°
2.16	30.86°	30.91°	22.7°	2.40	30.54°	30.61°	23.1°
2.18	30.82°	30.87°	22.6°	2.42	30.52°	30.60°	22.9°
2.20	30.79°	30.84°	22.8°	2.44	30.51°	30.58°	22.9°
2.22	30.76°	30.81°		2.46	30.50°	30.575°	23.0°
2.24	30.72°	30.775°	23.2°	2.48	30.50°	30.57°	23.1°
2.26	30.695°	30.755°	23.4°	2.50	30.495°	30.565°	23.0°
2.28	30.67°	30.73°	23.6°	2.52	30.49°	30.56°	
2.30	30.65°	30.71°	23.4°	2.54	30.46°	30.50°	
				3.09	30.23°	30.27°	23.05°

Cooling of calorimeters in 15 minutes, right 0.23°, left 0.23°. Feet out of calorimeters at 2.52.

Volume of right foot 834 c.c., of left 837 c.c. Water equivalent of calorimeters with contents, right 4,444 c.c., left 4,446 c.c. Rectal temperature 40.2° C.

Fourth Examination.—November 1, 1912. The patient's temperature is now about normal and he feels much better. The maximum and minimum temperatures were as follows:

October 16, 105.0° and 99.4° F. October 17, 103.4° and 100.4° F.
October 18, 104.0° and 100.4° F. October 19, 104.0° and 100.0° F.

Since October 19 the temperature has gradually fallen. On October 31 the maximum was 99.0° F. and the minimum 98.0° F.

Pulse (lying on back on the ambulance) 87. Feet in bath at 2.07 P.M., and in calorimeters at 2.21 P.M. 2,775 c.c. of water in each calorimeter. The calorimeters had been reduced in size since the last examination. The soles of the feet rest on the footrest as before. Consequently a smaller portion of the leg is now inside the calorimeter. Blood pressure, left arm, systolic 108, 84 (sound gone).

Time.	Temperature of Calorimeters.		Temperature of Room.	Time.	Temperature of Calorimeters.		Temperature of Room.	Notes.
	Right.	Left.			Right.	Left.		
2.23	30.56°	30.65°		2.45	30.24°	30.295°	22.0°	Feet out of calorimeters at 3.02.
2.25	30.495°	30.58°	21.4°	2.47	30.25°	30.30°	22.1°	
2.27	30.41°	30.52°	21.4°	2.49	30.265°	30.31°	22.15°	
2.29	30.37°	30.46°	21.5°	2.51	30.28°	30.32°	22.2°	
2.31	30.32°	30.43°	21.7°	2.53	30.305°	30.33°	22.25°	
2.33	30.29°	30.38°	21.8°	2.55	30.35°	30.345°	22.2°	
2.35	30.275°	30.355°	21.9°	2.57	30.365°	30.355°	22.3°	
2.37	30.26°	30.34°	21.9°	2.59	30.385°	30.365°	22.4°	
2.39	30.25°	30.33°	22.0°	3.01	30.395°	30.38°	22.4°	
2.41	30.235°	30.31°	22.0°	3.03½	30.34°	30.335°		
2.43	30.235°	30.30°	22.0°	3.25	29.97°	29.955°		

Cooling of right calorimeter in 21½ minutes 0.37°, of left 0.38°.
Volume of right foot in calorimeter 780 c.c., of left 740 c.c.
Water equivalent of right calorimeter and contents 3,560 c.c., of left 3,530 c.c.

The first examination of J. B. was made on October 2, 1912, ten days after his admission, more than four weeks from the beginning of his illness, and a week after the maximum temperature (105.8° F.) had been reached. The rectal temperature after the examination was 39.35° C. (102.83° F.). The flow in the feet was the largest observed in this series of fever cases and the only flow which fell within the normal range (3.36 grams per 100 cubic centimeters per minute for the right foot, and 3.82 grams for the left, with room temperature 24.4° C.).

Six days later, his temperature having meanwhile mounted again and continued high, the foot flow was found to be much smaller (table II, footnote), and eight days later, on October 16, the rectal temperature being now 40.2° C. (104.36° F.) the flow was only 0.80 grams for the right foot and 0.74 grams for the left. The clinical records show great variations in temperature since the first examination and he continued to present disturbing symptoms, cardiac and otherwise.

The last examination was made on November 1, 1912, almost seven weeks after admission to the hospital and ten weeks after the beginning of the illness, his temperature being now for the first time fairly stable and at a normal level. The flow was 2.08 grams per 100 cubic centimeters per minute for the right foot and 1.89 grams for the left. In view of the fact that the room temperature was more than 2° C. lower on this than on the first occasion, the results indicate that at the first examination the conditions that determine the rate of flow in the feet were more similar to the conditions at the last examination than to those at the two intermediate examinations, in spite of the great difference of body temperature. The most natural explanation is that both at the first and the last examination in this rather protracted case the intoxication was subsiding and the cutaneous vasoconstriction was disappearing. After the first examination, however, a relapse seems to have occurred, the patient's progress being interrupted by complicating incidents (continued ulceration, etc.), the cutaneous vasoconstriction increased, and the temperature ran up again almost, if not quite, to the maximum reached before. In the absence of simultaneous measurements of the hand flow it is impossible to know whether intoxication of the heart contributed to the smallness of the foot flows in the intermediate period, although from the heart symptoms this seems probable. The progressive diminution in the volume of the feet in the first three examinations is a point which may be noted since it affords a quantitative expression (for a particular part) of the increasing emaciation which was very evident in the body as a whole. The foot volume at the fourth examination is not comparable with the others as the reduced calorimeters were then used for the first time.

In F. B., a case of pneumonia, the flow at the first examination, on the day of his admission to the hospital and a fortnight from the beginning of his illness, was 2.07 grams per 100 cubic centimeters of foot per minute for the right foot, and 2.30 grams for the left, with room temperature 23.0° C.,—flows not perhaps markedly deficient for his age, but certainly not above the normal. Six days later the flow was less (1.36 grams for the right, and 1.12 grams for the left foot) with a slightly lower room temperature, but practically the same rectal temperature. Here again in the absence of observations on the hands it cannot be stated what share the weakening of the heart might have had in the diminution of the flow. That it was weakening at this time is probable, as he died four and a half days later, apparently from a general intoxication.

F. B.—A man, aged 53½ years, a cook by occupation, was admitted to the City Hospital on December 5, 1912, with lobar pneumonia, the lower lobe of the left lung being consolidated. His illness began two weeks before admission, with pain in the left side, chills, and fever. Cough and shortness of breath developed shortly after. But he did not go to bed, and indeed he walked into the hospital. The maximum and minimum temperatures were:

December 6, 103.8° and 103.0° F.
December 7, 104.0° and 102.6° F.
December 8, 103.8° and 102.6° F.
December 9, 103.2° and 101.0° F.
December 10, 103.0° and 101.2° F.

The leucocyte count was as follows:

December 6	8,600
December 7	12,400
December 8	18,400
December 9	20,400

On December 5 the blood flow in the feet was measured while the patient lay on his back. Pulse 92. Feet in bath at 2.04 P.M., and in calorimeters at 2.16 P.M. 2,775 c.c. of water in each calorimeter. The calorimeters of reduced capacity were used.

Time.	Temperature of			Time.	Temperature of calorimeters.		Notes.
	Calorimeters.		Room.				
	Right.	Left.			Right.	Left.	
2.14	31.49°	31.65°	23.7°	2.28	31.67°	31.87°	Room temperature 22.7°.
2.18	31.46°	31.63°	23.8°	2.30	31.71°	31.925°	
2.20	31.50°	31.69°	23.5°	2.32	31.77°	31.97°	Feet out of calorimeters at 2.32.
2.22	31.54°	31.755°	22.9°				
2.24	31.59°	31.79°	22.9°	2.34	31.765°	31.955°	
2.26	31.62°	31.84°	22.8°	2.49	31.50°	31.695°	

Cooling of right calorimeter 0.265° in 15 minutes, of left 0.265°.
Volume of right foot 1,081 c.c., of left 1,044 c.c. Rectal temperature 39.4°.

Blood pressure, left arm, systolic 104 (stethoscope), 103 (palpation); 84 (sudden decrease in sound), 58 (sound gone).

At the second examination of F. B. on December 11, 1912, the feet were put into the bath at 1.55 P.M., and into the calorimeters at 2.11½ P.M. Pulse (lying on back, as in the previous examination) 112. 2,775 c.c. of water in each calorimeter, the calorimeters of reduced capacity being used.

Time.	Temperature of			Time.	Temperature of calorimeters.		Notes
	Calorimeters.		Room.				
	Right.	Left.			Right.	Left.	
2.09	31.25°	31.17°		2.29	31.28°	31.13°	
2.14	31.15°	31.07°		2.31	31.295°	31.135°	Room temperature 22.1°.
2.17	31.17°	31.08°	21.0°	2.33	31.305°	31.14°	Room temperature 22.1°.
2.19	31.19°	31.085°	21.3°	2.35	31.325°	31.14°	Feet out of calorimeters at 2.35.
2.21	31.205°	31.095°	21.7°				
2.23	31.22°	31.11°	21.8°	2.37½	31.29°	31.09°	
2.25	31.25°	31.12°	21.8°	2.50½	31.06°	30.86°	
2.27	31.265°	31.13°	21.9°				

Cooling of right calorimeter 0.23° in 13 minutes, of left 0.23°.
Volume of right foot 1,072 c.c., of left 1,023 c.c. Rectal temperature 39.3°.

Water equivalent of calorimeters and contents, right 3,779 c.c., left 3,742 c.c. The patient died on December 15, the whole left lung being consolidated before death. The systolic blood pressure was 96 on December 12, 80 on December 13, and 90 on December 14, all the observations being taken in the afternoon.

TABLE I.

	Date.	Heat given off per min. in small calories.		Heat given off per 100 c.c. of foot per min.		Heat given off per gm. of blood.		Rectal temperature.
		Right.	Left.	Right.	Left.	Right.	Left.	
Normal Individuals.								
M.C.	May 2, 1911	251.6	—	20.6	—	5.77	—	37.4°
	May 18, 1911	211.6	—	17.4	—	4.93	—	37.5°
	June 17, 1911	332.3	278.8	28.4	25.6	5.76	6.06	37.6°
	Mar. 26, 1913	290.2	290.2	23.5	24.2	4.60	4.64	37.1°
C.B.	May 2, 1911	262.1	—	26.7	—	5.65	—	36.9°
J.R.	Mar. 25, 1913	351.7	327.1	34.8	34.1	4.37	4.49	37.0°
N.R.	Apr. 8, 1913	83.8	70.6	17.0	14.7	5.05	5.14	37.2°
Fever Patients.								
F.B.	Dec. 5, 1912	145.0	151.5	13.4	14.5	6.41	6.29	39.4°
	Dec. 11, 1912	98.0	78.4	9.1	7.6	6.69	6.83	39.3°
J.B.	Oct. 2, 1912	211.3	240.0	22.7	25.3	6.78	6.63	39.35°
	Oct. 16, 1912	54.7	50.2	6.5	6.0	8.18	8.12	40.2°
	Nov. 1, 1912	95.7	81.6	12.2	11.0	5.87	5.81	37.45°
M.V.	Oct. 8, 1912	163.0	157.9	12.3	12.2	8.00	8.13	40.5°
	Nov. 5, 1912	81.8	90.8	7.3	8.2	5.91	5.87	37.95°
F.S.	Oct. 2, 1912	94.7	90.2	7.3	7.1	4.97	5.13	37.9°
F.D.	Oct. 1, 1912	56.8	49.1	4.1	4.3	5.12	5.19	37.2°

TABLE II.

	Date.	Age in yrs.	Pulse rate.	Blood pressure.	Temperature of				Volume of part in c.c.		Heat given off in small calories.			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.											
							Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
								Normal Individuals.										
M. C. Hands.	May 4, 1911	22	90		23.3°	36.7°	30.04°	30.03°	486	470	3,380	2,950	9	62.48	54.60	12.86	11.61	Left forearm bandaged befo experiment and bandage r moved.
	May 24, 1911		87		27.0°	36.8°	30.91°	30.91°	470	457	3,228	2,976	7	86.99	80.20	18.51	17.55	
	Nov. 2, 1911		76		22.2°	36.5°	29.78°	29.77°	465	435	884	878	3	48.72	48.31	10.48	11.10	Cuff on right arm, but pressure.
	Nov. 3, 1911		88	115	25.1°	36.75°	30.01°	30.04°	493	459	1,815	1,627	5	59.84	53.88	12.14	11.74	Cuff on right arm, but pressure.
	Nov. 9, 1911		87	115	24.1°	36.7°	30.84°	30.88°	465	465	2,357	2,046	7	63.84	55.80	13.73	12.0	12.54 allowing for swelling left hand.
	Nov. 15, 1911		—	113, 85	25.2°	36.8°	30.79°	30.83°	480	461	2,932	2,737	8	67.53	63.68	14.07	13.81	
	Nov. 27, 1911		100	124	21.4°	36.9°	29.92°	29.87°	477	455	1,617	1,356	7	36.77	30.57	7.71	6.72	
	Dec. 11, 1911		74	122, (92), 82	24.5°	36.6°	31.18°	31.12°	450	444	2,315	2,225	8½	55.83	53.17	12.41	11.98	
	Mar. 26, 1913	24	97		24.5°	36.6°	31.53°	31.61°	505	485	2,712	2,612	8	74.29	73.28	14.71	15.10	
					24.5°		32.27°				3,289		14	60.24		11.93		Left hand in cold water.
					24.6°		32.73°				507		3	48.52		9.60		Left hand in warm water.
					24.5°		33.10°				1,889		8	74.96		14.84		Left hand still in warm wate
M. C. Feet.	May 2, 1911	22			25.25°	36.8°	30.38°		1,220		1,510		6	43.55		3.57		Foot at rest.
					25.4°		30.55°				1,253		5	44.55		3.65		Working foot.
					25.2°		30.71°				1,437		6	43.69		3.58		Foot at rest.
	May 18, 1911		76		26.4°	36.9°	31.42°		1,210		2,116		10	42.90		3.54		
	June 17, 1911		84		21.8°	37.0°	30.60°	30.26°	1,170	1,085	3,988	3,346	12	57.69	45.97	4.93	4.24	
	Mar. 26, 1913	24	92		24.5°	36.5°	31.38°	31.34°	1,232	1,195	4,064	4,064	14	62.99	62.50	5.11	5.23	Lying on back.
			98		24.5°		32.06°	32.03°			3,119	3,212	16	48.78	49.90	3.96	4.17	Sitting.
					24.6°			32.46°				1,355	10		37.26		3.12	Right foot in cold water.
					24.6°			32.76°				1,664	8		61.79		5.17	Right foot still in cold water.
					24.6°			32.84°				930	6		47.05		3.93	Right foot in warm water.
					24.6°			33.16°				2,747	10		91.38		7.64	Right foot still in warm wate

	Date.	Age in yrs.	Pulse rate.	Blood pressure.	Temperature of				Volume of part in c.c.		Heat given off in small calories.			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.		Right.	Left.	Right.	Left.	In min.	Rght.	Let.	Right.	Left.	
							Right.	Left.										
Normal Individuals.																		
C. B. Hands.	May 22, 1911	22	80		28.9°	36.6°	31.15°	31.21°	415	410	3,975	4,176	16	50.65	53.83	12.20	13.13	
					29.0°		31.76°				497		4	28.52		6.95		Left hand in cold water.
					29.0°		31.96°				1,028		6	41.03		9.89		Left hand still in cold water.
					29.1°		32.36°				2,022		11	48.17		11.60		Left hand in warm water.
	Nov. 17, 1911		106	103	24.9°	36.5°	30.15°	30.29°	430	424	2,338	2,712	8½	49.22	57.09	11.45[1]	13.46[1]	
	Nov. 20, 1911			113	24.8°	36.45°	30.68°	30.66°	410	405	1,369	1,334	10	26.36	25.55	6.43[1]	6.30[1]	
	Nov. 21, 1911		104	115	24.2°	36.75°	31.28°	31.36°	410	405	2,096	2,060	9	47.30	46.83	11.54[1]	11.4 [1]	
	Nov. 24, 1911		80	116	23.5°	36.6°	30.48°	30.40°	400	385	785	953	6	23.56	28.46	5.89[1]	7.39[1]	Hands felt cold though not to the subject.
C. B. Foot.	May 2, 1911		72		26.3°	36.3°	30.02°		980		1,573		6	46.38		4.73		Foot at rest.
					26.3°		30.20°				1,145		4	52.14		5.32		Working foot.
					26.0°		30.36°				1,216		4	56.82		5.79		Foot at rest.
J. R. Hands.	Mar. 22, 1913	20	52		24.0°	36.0°	30.90°	30.88°	397	354	2,388	1,537	13	40.02	25.66	10.08	7.25	
					24.2°		31.30°				1,092		13	19.85		5.00		Left hand in cold water.
					23.95°		31.42°				113		2	13.70		3.45		Left hand in warm water.
					23.9°		31.49°				409		3	33.59		8.46		Left hand still in warm water.
					23.95°		31.72°				1,610		7	59.70		15.04		Left hand still in warm water.
	Mar. 25, 1913		62	101, 60	24.8°	36.5°	31.62°	31.55°	393	376	3,206	2,217	15	48.66	33.17	12.38	8.82	
					24.4°		32.11°				460		5	23.28		5.92		Left hand in cold water.
					24.4°		32.25°				802		5	41.93		10.67		Left hand still in cold water.
					24.4°		32.37°				347		3	31.11		7.91		Left hand in warm water.
					24.5°		32.61°				1,699		7	69.32		17.64		Left hand still in warm water.
J. R. Feet.	Mar. 25, 1913		76		25.1°	36.4°	31.54°	31.40°	1,008	959	4,925	4,580	14	80.42	72.70	7.98	7.58	Lying on back.
					24.6°		32.60°	32.34°			4,869	4,359	18	79.09	66.27	7.84	6.90	Sitting.
					24.5°			32.87°				1,440	10		45.32		4.72	Right foot in cold water.
					24.45°			33.08°				1,405	8		58.77		6.12	Right foot in warm water.
					24.45°			33.35°				1,753	8		79.82		8.27	Right foot still in warm water.

TABLE II.—*Continued.*

	Date.	Age in yrs	Pulse rate.	Blood pressure.	Temperature of				Volume of part in c.c.		Heat given off in small calories.			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.		Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
							Right.	Left.										
							Normal Individuals.											
N. R.	Apr. 8, 1913	8¾	84		24.0°	36.7°	30.97°	31.10°	203	181	1,292	1,226	15	16.70	16.21	8.22	8.95	Hands.
					24.0°	36.6°	30.98°	30.88°	491	480	1,509	1,272	18	16.57	13.72	3.37	2.86	Feet.
							Fever Patients.											
F. B.	Dec. 5, 1912	53½	92	104, 58	23.0°	38.8°	31.62°	31.80°	1,081	1,044	2,176	2,273	15	22.45	24.05	2.07	2.30	Pneumonia. Feet.
	Dec. 11, 1912		112		22.0°	38.7°	31.24°	31.11°	1,072	1,023	2,059	1,646	21	14.63	11.47	1.36	1.12	
J. B.	Oct. 2, 1912	24	108	100, 78	24.4°	38.75°	31.21°	31.38°	927	945	3,382	3,840	16	31.15	36.18	3.36	3.82	Typhoid. Feet.
	Oct. 8, 1912		104	109, 65	22.2°	38.85°	30.36°	30.35°	924	900	—	—	—	—	—	—	—[2]	
	Oct. 16, 1912		106	104, 66	23.0°	39.6°	30.50°	30.58°	834	837	547	502	10	6.68	6.18	0.80	0.74	
	Nov. 1, 1912		87	108, 84	22.2°	36.85°	30.32°	30.34°	780	740	1,531	1,306	16	16.28	14.04	2.08	1.89	
M. V.	Oct. 8, 1912	29	108	118, 89	22.2°	39.9°	30.97°	30.86°	1,322	1,294	2,292	2,211	14	20.37	19.41	1.54	1.50	Typhoid. Feet.
	Nov. 5, 1912		80	107, (92) 65	22.9°	37.35°	30.80°	30.82°	1,109	1,100	1,145	1,272	14	13.82	15.45	1.24	1.40	
F. S.	Oct. 2, 1912	28	72	100, (77), 58	24.1°	37.3°	31.77°	31.59°	1,295	1,258	2,180	2,076	23	19.04	17.56	1.47	1.39	Typhoid. Feet.
F. D.	Oct. 1, 1912	26	81	108, 84	22.9°	36.7°	31.91°	31.88°	425	423	1,511	1,426	9	38.94	36.50	9.16	8.63	Typhoid (convalescent). Hands, feet.
					22.45°	36.6°	30.90°	30.82°	1,135	1,117	910	787	16	11.08	9.45	0.98	0.85	
J. McD.	May 16, 1912	26	80		23.2°	36.7°	31.28°	31.52°	511	505	3,118	3,568	18	35.51	42.52	6.95	8.42	Typhoid (convalescent). Hands.
					23.2°			31.99°				654	5		30.83		6.10	Right hand in cold water.
					23.1°			32.14°				833	5		40.59		8.04	Right hand still in cold water.
					23.3°			32.34°				1,242	10		31.65		6.26	Right hand in warm water.

[2] The flow was so small that even after the feet had been in the calorimeters for 21½ minutes the loss of heat by the calorimeters to the room was not yet balanced. The feet were withdrawn before usable readings were obtained. From the readings obtained it is practically certain that the foot flow was not greater than on October 16.

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CONCLUSIONS.

1. In the cases of fever investigated the flow in the feet never exceeded the normal flow and was usually much below the normal

2. In explanation of the relatively small foot flow in the fever cases it is suggested that the vasoconstrictor mechanism of the peripheral parts, especially of the skin, is abnormally excited, and some direct evidence that this is the case is brought forward.

3. The significance of this hypersensitiveness, or at least increased action, of the cutaneous vasoconstrictor mechanism is assumed to be that the peripheral vasoconstriction is a compensatory arrangement which secures for the organs mainly suffering from the infective process an increased flow of blood.

4. On this hypothesis the rise of temperature is, chiefly at least, secondary, inevitably following the vasoconstriction, provided that the metabolism is, upon the whole, not diminished.

5. Accordingly the rational treatment of hyperpyrexia, or of pyrexia if it is considered necessary to treat it, is to abstract heat by a process which will not diminish and may even increase the cutaneous vasoconstriction. This condition is exactly fulfilled by the cold bath, at least as regards its initial effect. Other so called tonic effects of the cold bath are not considered here.

Antipyretic drugs which act by dilating the cutaneous vessels would seem to be inferior in this regard. They diminish the temperature, it is true, but at the cost of defeating the beneficial redistribution of the blood which it is the function of the peripheral vasoconstriction to insure.

6. It is obvious that for the elimination of a given quantity of heat from the skin by radiation and conduction[3] in fever, a smaller cutaneous blood flow will suffice than with normal body temperature, since the elimination of heat per gram of blood passing through the surface must be greater in fever owing to the greater difference of temperature between the surface of the body and its surroundings.

I am much indebted to the staff of the City Hospital for their coöperation which has rendered this investigation possible.

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[3] Loss of heat by sweat is not considered since the parts investigated could not lose heat in this way under the conditions of the observations.

Studies on the Circulation in Man

IX. THE BLOOD-FLOW IN THE HANDS (AND FEET) IN CASES IN WHICH OBVIOUS ANATOMICAL DIFFERENCES EXIST

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STUDIES ON THE CIRCULATION IN MAN

IX. THE BLOOD-FLOW IN THE HANDS (AND FEET) IN CASES IN WHICH OBVIOUS ANATOMICAL DIFFERENCES EXIST *

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In this paper and succeeding ones I propose to continue the description and discussion of the results obtained in clinical cases already begun[1] in papers VI and VIII.

GENERAL REMARKS

A portion of the material studied consisted of patients in the Dispensary of Western Reserve University and Lakeside Hospital, referred to in the protocols simply as the Dispensary. The major portion of the material was from the wards of the City and other hospitals. A few cases were placed at my disposal from the private practice of friends. This is pointed out because comparable results are much more easily obtained in successive observations on hospital patients whose surroundings are fairly constant, than on dispensary or private patients. At any rate, in order to obtain comparable results, fewer precautions are necessary in the case of the hospital patients. In particular, the influence of the external temperature, the factor which of all others among the external conditions is most apt to influence the results, is much more easily controlled in the case of the hospital patients, especially in winter. The observations on the latter were made in a room in the hospital to which the patients were brought in the wheel chair, or the movable bed; or to which, if well enough, they walked. As is true for many kinds of physiological clinical examination, the observations are more satisfactorily made in a separate room than in the open wards. Where the external conditions are controlled and the clinical state of the patient has not altered noticeably, the results of the blood-flow measurements from day to day, or indeed from week to week, show a very fair and often a surprising degree of constancy. Not only is the hospital patient in an environment whose temperature varies comparatively little, but his diet is also controlled and the general régimen under which he lives is relatively stable. In many of the hospital cases the approximate constancy of the flow was not only seen in the case of

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* From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University.

[1] Stewart, G. N.: Jour. Exper. Med., 1913, xviii, Nos. 2 and 4.

one and the same hand, but also in the proportion between the flows in the two hands where a conspicuous difference existed between the two. As regards the dispensary material, care had to be taken in winter that the person was long enough in the room before the observations were begun, especially if he came to the dispensary with bare hands. It is true that if the observations were immediately begun a result would be obtained which would be correct enough for the given condition of the hands, but it would be useless as an expression of the flow under the approximately standard conditions which have to be established if comparison of the flow in the same patient at different times or in different patients is proposed. In summer the factor of external temperature presents no greater difficulty in dealing with dispensary than with hospital patients.

In addition to the clinical interest which attaches to the measurements in the individual cases dealt with in this paper, the material was chosen partly as a test of the technic of the method, as in many of the cases the qualitative difference between the two hands could be foreseen from the anatomical difference which existed.

In Steve S., a man 21 years old, with healing burns on both hands, but more extensive on the right, the flow was 7.04 grams per 100 c.c. per minute for the right hand and 5.44 grams for the left hand (for the last nine minutes in the calorimeters), with an average room temperature of 25. The burned areas on both hands were quite red, and taking the whole surface of the hands into account the vascularity of the superficial layers must have been considerably greater in the right than in the left hand. In both hands many blood-vessels in the new tissue must be nearer the surface than in the normal hand, a point of interest in connection with the technic of the method.[2] In spite of the red color, both hands feel rather cold to the touch, and this agrees perfectly with the tardiness[3] with which the thermometers rose at first and with the calculated blood-flow, which for the man's age and the room temperature, is subnormal. The redness is due to the number of capillaries in the healing areas and the fact that they lie just under the surface, not to a great flow of blood through widely dilated vessels. The case presented the opportunity of studying the flow in blood-vessels which have not long existed and whose vasomotor connections may be still incomplete or immature. Immersion of the left hand in warm water caused a good increase, and subsequent immersion of the left hand in cold water a marked decrease in the flow in the right hand. The persistence of both reflexes was remarkable. Another peculiarity not observed in any other case was that the temperature of the right hand calorimeter during the immersion of the left hand in the warm or cold water, showed abrupt changes, for instance, a sudden rise of the thermometer between the third and fourth minutes of immersion of the left hand in the cold water — not succeeded by any further rise. The patient denied that his hand ever touched the thermometer, and from the position of the thermometer in the calorimeter contact of the hand with it can scarcely occur, unless the hand is executing extensive groping movements, of which there was no sign in these observations. The most plausible explanation of the phenomenon would

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[2] Heart, 1911, iii, 55.

[3] This tardiness is expressed in the calculated flow for the first eight minutes of immersion in the calorimeters, which is only 3.74 grams per 100 c.c. per minute for the right, and 2.49 grams for the left hand. The fact that the ratio of the flow in the left hand to that in the right is 1:1.50 for the first eight minutes, while it is 1:1.29 for the last nine minutes, in the calorimeters, indicates clearly that the increase in flow in the last period was not due to a central cause (increase in the driving power of the heart) which would have affected the two hands equally, but to a peripheral cause (removal of vasoconstriction which happened to be proportionately greater in the left hand at the beginning of the immersion in the calorimeters than later on).

TABLE 1.—Calorimeter Test of Steve S.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
3:33½	29.92	29.84	.....	3:55	30.32	
3:37	29.90	29.88	.....	3:56	30.37	Room 24.8 C.
3:38	29.91	29.90	25.3	3:57	30.495	
3:39	29.92	29.905	.....	3:58	30.505	
3:40	29.93	29.915	.....	3:59	30.53	
3:41	29.95	29.925	.....	4:00	30.64	
3:42	29.97	29.925	.....	4:01	30.64	
3:43	29.99	29.93	25.0	4:02	30.67	
3:44	30.01	29.935	.....	4:03	30.75	
3:45	30.015	29.945	.....	4:04	30.82	Room 24.9 C.
3:46	30.05	29.97	.....	4:05	30.86	
3:47	30.10	29.99	.....	4:06	30.88	At 4:06 left hand put in water at 10 C.
3:48	30.11	30.025	.....	4:07	30.87	
3:49	30.16	30.05	.....	4:08	30.88	Room 24.8 C.
3:50	30.20	30.07	24.6	4:09	30.89	
3:51	30.215	30.12	.....	4:10	30.99	
3:52	30.28	30.14	.....	4:11	30.98	
3:53	30.295	30.15	.....	4:12	30.97	
3:54	30.305	30.18	.....	4:13	30.98	
....	.....	.....	.....	4:14	30.995	Hand out of cal. at 4:14.
....	.....	.....	.....	4:27	30.88	At 4:27 L. is at 29.94 C. Room 24.2 C.

Cooling of calorimeters, R., 0.115 degrees in thirteen minutes; L., 0.24 degrees in thirty-three minutes. Volume of right hand in calorimeter, 328 c.c.; left, 340 c.c. The hands, especially the right, could not be made to hang vertically in the calorimeters owing to adhesions. The volumes given represent the portions of the hands actually inside the calorimeters. Water equivalent of calorimeters with contents, R., 3,357; L., 3,367. Rectal temperature, 37.3 C.

seem to be that in the new blood-vessels, although the vasomotor connections had been established, there is still an abnormal vasomotor instability. The intensity of the total reaction may be due either to hyperexcitability of the receptive surfaces of the left hand (afferent path) or to hyperexcitability of the newly-formed vasomotor endings including the muscle of the new blood-vessels (efferent path) or to both. The warm water was purposely made 3 degrees lower, and the cold water 2 degrees higher than usual, lest pain should be caused. But he did not feel any pain.

Steve S., aged 21, a sailor, was burned November 4, 1911, by the bursting of a steam pipe on a steamer. He was unconscious for a fortnight. The face, including the ears, the neck, the back, the knees and both hands and arms were burned. The sight of the right eye was destroyed. He was admitted to the City Hospital Feb. 19, 1912. Both forearms and a small portion of the upper arms above the elbow were denuded of skin and covered with jelly-like exudation and granulations. Physical examination of the heart and lungs was negative.

The blood-flow in the hands was measured April 5, 1912, at which time healing was pretty well completed, although there was still some suppuration on the right forearm, a little above the wrist. The burn on the right hand involved the palms as well as the back of the hand and there are considerable adhesions between the fingers, rendering the hand practically useless. The left palm escaped in great measure, but the back of the hand was burned. The burned areas on the hands were still quite red. Hands in bath at 3:24 p. m., in calorimeters at 3:34½; 3,015 c.c. of water in each calorimeter.[4] At 3:54 p. m. left hand put into water at 40 C. Pulse 80.

In Frank P., a man 42 years old, suffering from a malignant tumor of the right forearm, with some edema of the forearm down to the wrist, the flow in the right hand was 4.69 grams per 100 c.c. of hand per minute, in the left hand 5.31 grams, with an average room temperature of 23.2 C. The deficiency in the right hand was an actual deficiency and not merely an apparent one (owing to the reckoning in of edema liquid in the volume of the hand), since by measurement the right hand was only 3 c.c. larger than the left. It is therefore probable that the deficiency is due to the interference of the tumor with the venous return from the hand. Insofar as it is not connected with inflammatory changes, the edema is also probably caused by interference with the venous flow. In certain cases the blood-flow measurement might help to settle the question whether edema is due to obstruction on the lymph path or on the venous path. Obstruction confined to the lymphatics might cause edema without diminution in the blood-flow. Where a tumor is confined to the bone, obstruction to the flow of blood in the hand may be expected to be less marked than where it has extensively invaded the soft tissues.

Frank P., a carpenter, aged 42, was admitted to the City Hospital July 18, 1912, with a tumor mass about 10 cm. in diameter on the outer surface of the right forearm. The mass was slightly fluctuant, tender on pressure and attached to the bone. There was some edema in the right forearm and wrist. There was another tumor mass over the upper third of the left tibia about 15 cm. in diameter. It had been incised for drainage and a muco-purulent fluid was being discharged. There was a small mass and tenderness over the upper third of the right fibula. X-ray examination showed a large rounded mass on the right forearm going deep into the tissues, as much of it below the surface as above the surface. The swellings on the left leg and upper forearm were noticed about the same time, three months before admission. They have gradually increased in size and of late have been very painful. Physical examination of the heart was negative. Thorax emphysematous and expiration prolonged. Percussion note raised in pitch and shortened on the left side, especially at the left base. Respiratory sounds diminished on the left side, where numerous rhonchi were present. Tactile fremitus diminished on the left side. The diagnosis was multiple sarcoma. The patient refused operation and left the hospital. The examination of the blood-flow was made Aug. 1, 1912. Hands in bath at 2:22 p. m., in calorimeters at 2:33 and out of calorimeters at 2:52. Pulse (sitting) 96. The day was exceptionally cool for the season.

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[4] In all observations on the hands unless otherwise stated, this was the quantity of water in each calorimeter.

TABLE 2.—CALORIMETER FINDINGS IN CASE OF FRANK P.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp., C.
2:32	30.16	30.14	....	2:44	30.48	30.49	23.4
2:34	30.18	30.15	22.9	2:45	30.505	30.54	....
2:35	30.205	30.175	.....	2:46	30.53	30.58	23.2
2:36	30.23	30.20	23.1	2:47	30.57	30.62	....
2:37	30.26	30.21	.....	2:48	30.595	30.665	....
2:38	30.27	30.26	23.1	2:49	30.61	30.69	....
2:39	30.315	30.29	.....	2:50	30.64	30.72	23.0
2:40	30.35	30.33	23.1	2:51	30.67	30.75	....
2:41	30.39	30.37	.....	2:52	30.695	30.765	22.95
2:42	30.41	30.43	.....	3:09	30.485	30.565	....
2:43	30.44	30.46	.....	....	......	......	....

Cooling of calorimeters in seventeen minutes, R., 0.21 degrees; L.. 0.20 degrees. Volume of right hand, 476 c.c.; the same for a second measurement. Volume of left hand, 473 c.c. To the eye the right hand appeared somewhat swollen, but this seemed to be an error of judgment, caused by the distinct swelling of the right forearm below the level of the tumor down to and involving the right wrist. The swelling did not descend below the wrist. Water equivalent of calorimeters with contents, R., 3,476; L., 3,473. Blood-pressure, left arm, systolic 115 (palpation), 114 (stethoscope), 80 (sound gone). Pulse (sitting) 114. Rectal temperature, 37.95 C.

A condition in which edema coincided with obstruction to the lymph-flow not involving the venous flow seems to have been realized in the case of Charles B., a man 47 years old, in whom the diagnosis of Hodgkin's disease was made. He entered the hospital with both legs and feet greatly swollen. The swelling was stationary and little if at all diminished in the morning. During his entire stay in the hospital (over five weeks) the swelling of the legs remained unchanged. There was no edema elsewhere. All accessible lymph-nodes were enlarged. The blood-flow in the right foot was 2.34 grams per 100 c.c. of foot per minute, or, allowing for the edema fluid, 3.04 grams, and in the left foot, 2.50 grams (allowing for the edema fluid, 3.24 grams) with average room temperature 22.5 C. These flows are by no means small for the feet. Indeed, in comparison with the hand flows (2.82 grams for the right and 3.22 grams for the left hand) they are large. A certain degree of anemia, some cyanosis and dyspnea were present, and this may contribute to the small hand flow.[5] It may be supposed that this would tell equally on the blood-flow through the feet, but in the absence of special observations on this point, we cannot be certain whether the compensatory vasoconstriction in anemia is not greater in the anterior limb than in the posterior limb. It is conceivable that the circulation in the anterior limb has a closer association with the pulmonary circuit than the circulation in the posterior limb. That the hands were exceptionally liable to vasoconstriction was shown by observations on Nov. 27, 1912, which gave a still smaller flow. It is rare to find a case in which the flow per 100 c.c. of foot per minute comes out as great as the flow per 100 c.c. of hand per minute in the same individual. In the vast majority of clinical cases the hand flow greatly preponderates, and this is the invariable rule for normal persons so far as our experience goes.[6]

Interference with the local circulation would seem to be excluded in this case as a cause of the edema of the legs. It is more likely, indeed, if we take account of the hand flows, that there is a local acceleration of the blood flow in the legs, perhaps through partial paralysis of their vasoconstrictors by the pressure of the same masses, if it is an affair of mechanical pressure, as are responsible for the edema. If we confine ourself to the question, leaving out all other possibilities, whether the edema is dependent on venous or on lymphatic obstruction, the blood flow measurements give an answer in favor of lymphatic obstruction, to this extent supporting the diagnosis of Hodgkin's disease.

Charles B., lumberman, 47 years old, height 5 feet, 6 inches, was admitted to City Hospital November 8, 1912. The glands were generally enlarged, one of the inguinal glands on the left side being as big as a walnut. Both legs were edematous and covered with varices. The varicose veins, however, were of a good many years' standing, and had not increased during the present illness, which began two months before admission with pain in the back and shortness of breath. About two weeks before admission the pain recurred and he almost fainted with the pain in the back. The feet began to swell two days before admission; the left leg began to swell two days later than the right. No edema elsewhere than in the legs. He had always lived in Cleveland or the neighborhood. Has never had piles. The pain in the back was a cutting pain on both sides. There had never been gravel in the urine. The skin and mucous membranes showed slight anemia, slight cyanosis, no icterus. Thorax barrel-shaped, moves slightly more on the right side. The costal angle is obtuse, the breathing mainly abdominal. Further examination of thorax and the heart, also of the abdomen and rectum, negative. X-ray examination of abdomen negative. Some sclerosis of the radial artery. The reflexes were active. The urine contained albumin with a few granular casts on November 9, a trace only of albumin on November 18. On November 14 the leukocyte count was 14,000 (polymorphonuclear neutrophils 70 per cent., eosinophils 4.5 per cent., large mononuclears 5.5 per cent., small mononuclears 15 per cent., transitionals 2.5 per cent.).

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[5] Stewart: Paper VI, Jour. Exper. Med., 1913, xviii, No. 2.

[6] Stewart, G. N.: Paper VII, Jour. Exper. Med., 1913, xviii, No. 4.

TABLE 3.—Calorimeter Findings in Charles B. (Feet)

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
2:30	31.24	31.28	.....	2:47	31.38	31.465	.....
2:33	31.16	31.23	.....	2:49	31.40	31.485	22.7
2:35	31.19	31.27	.....	2:51	31.43	31.53	22.9
2:37	31.22	31.30	21.5	2:53	31.465	31.565	22.5
2:39	31.25	31.325	21.9	2:55	31.49	31.58	.....
2:41	31.29	31.365	22.1	2:57	31.42	31.55	.....
2:43	31.32	31.395	22.2	3:14	31.04	31.16	.....
2:45	31.335	31.44	22.4	....	.....	.....	.....

Cooling of calorimeters in seventeen minutes, R., 0.38 degrees; L., 0.39 degrees. Volume of right foot 1,313 c.c., of left foot 1,313 c.c. His feet were naturally not large, requiring a No. 7 shoe. Water equivalent of each calorimeter with contents, 3,694.

Hands in bath at 3:17 p. m., in calorimeters at 3:26½ and out of calorimeters at 3:45.

TABLE 4.—Calorimeter Findings in Charles B. (Hands)

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
3:25	30.80	30.73	.....	3:37	30.805	30.765	23.5
3:28	30.77	30.705	21.8	3:38	30.805	30.77	22.9
3:29	30.775	30.71	21.9	3:39	30.81	30.78	22.8
3:30	30.775	30.73	.....	3:40	30.815	30.79	22.7
3:31	30.78	30.735	22.3	3:41	30.825	30.82	22.6
3:32	30.78	30.735	22.5	3:42	30.83	30.83	22.7
3:33	30.79	30.745	23.0	3:43	30.84	30.84	.....
3:34	30.795	30.745	23.4	3:44	30.85	30.85	.....
3:35	30.795	30.755	23.7	3:45	30.86	30.855	.....
3:36	30.80	30.755	23.7	3:53	30.75	30.75	.....

Cooling of calorimeters in eight minutes; R., 0.11 degrees; L., 0.105 degrees. Volume of right hand 480 c.c.; of left 462 c.c. Water equivalent of calorimeters with contents, R., 3,479; L., 3,465. Rectal temperature 36.9 C. Blood-pressure in left arm (Nov. 27, 1912), systolic 158 (palpation), 155 (stethoscope), 95 (sound gone).

The blood-flow in the feet and hands was measured Nov. 29, 1912. The swelling of the legs, the patient said, was stationary. The varicose veins could not be seen on account of the swelling. There was no pain in the back, but he had pain in the lower abdomen a little above the level of the groin when he walked any distance. Pulse (sitting) 98. Feet in bath at 2:06½ p. m.; in calorimeters at 2:31 and out of calorimeters at 2:55½; 2,575 c.c. of water in each calorimeter, as finally reduced in size.[7]

TABLE 5.—CALORIMETER MEASUREMENTS OF FEET IN CHARLES W.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
2:16	31.30	31.38	.....	2:43	31.35	30.92	.....
2:19	31.24	31.26	23.8	2:45	31.38	30.93	23.6
2:21	31.225	31.265	.....	2:47	31.41	30.945	23.4
2:23	31.21	31.11*	.....	2:49	31.44	30.955	23.8
2:25	31.21	31.055	23.3	2:51	31.475	30.975	24.1
2:27	31.205	31.02	.....	2:53	31.505	30.995	24.1
2:29	31.21	30.98	23.15	2:55	31.535	31.025	23.6
2:32	31.22	30.94	23.3	2:57	31.575	31.045	23.2
2:35	31.24	30.93	.....	2:59	31.60	31.07	.....
2:37	31.275	30.92	23.5	3:01	31.57	31.05	.....
2:39	31.295	30.92	24.0	3:14	31.37	30.87	.....
2:41	31.32	30.92	23.9	....	.....	.....	.....

* Stirring in L. had not been thorough till now for fear of hurting the foot.

Cooling of calorimeters in thirteen minutes: R., 0.20 degrees; L., 0.18 degrees. Volume of right foot 1,203 c.c., of left foot 1,103 c.c. Water equivalent of foot calorimeters with contents, R., 3,817, L., 3,747. Hands in bath at 3:24½ p. m., in calorimeters at 3:34 and out of calorimeters at 3:45.

TABLE 6.—CALORIMETER MEASUREMENTS OF HANDS OF CHARLES W.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
3:33	31.27	31.22	.....	3:41	31.67	31.605	.....
3:35	31.29	31.255	22.9	3:42	31.72	31.66	24.2
3:36	31.33	31.31	22.9	3:43	31.785	31.72	24.1
3:37	31.40	31.36	23.0	3:44	31.83	31.765	.....
3:38	31.465	31.425	23.25	3:45	31.895	31.82	.....
3:39	31.53	31.485	23.5	3:52	31.79	31.72	.....
3:40	31.60	31.55	23.9	....	.....	.....	.....

Cooling of hand calorimeters in seven minutes: R., 0.105 degrees; L., 0.10 degrees. Volume of right hand 486 c.c., of left hand 470 c.c. He is right handed. There is no difference, he says, in his hands, as to strength or otherwise, nor was there any difference at the time of the "strokes." Water equivalent of hand calorimeters with contents, R., 3,484, L., 3,471. Rectal temperature 37.9 C.

He was discharged Dec. 22, 1912, able to use the left foot better, he says, than for the previous seven years.

Charles W., a clerk, aged 42, was admitted to the City Hospital October 29, 1912. He had rheumatism at the age of eight years, since which time the left leg seemed to be weaker and smaller than the right. At that time the arms and legs were somewhat swollen and extremely sensitive. He had a stroke of paralysis in 1903. He was sitting in a chair reading and found he could not rise to walk. There were no convulsions. Both arms and legs were affected. He could not move the eyes, nor talk, and his sight was affected. No bowel or bladder trouble. In seven months he had recovered from the stroke and had no trouble in walking or in any other way until 1907, when he had a second stroke of the same kind preceded by slight dizziness, but otherwise no subjective signs. There was no disturbance of vision. It took four years for his complete recovery from the second attack and then he felt "real well." Four months before admission he fell on the sidewalk and abraded the left shin about 3 inches. It healed somewhat and the scab "raised up" and began to pain him severely, the pain shooting down the leg. He went to a hospital for four weeks and it again healed to some extent. On leaving the hospital it became worse, then healed again, but continued to be very painful. It opened again and the pain continued so that he could not sleep. There are many petechial spots on the left leg. Examination of thorax negative. Reflexes increased in the left leg. The left leg is atrophied and much smaller than the right and 1½ inches shorter. The left foot is not small, although doubtless smaller than the right. It is the lower leg which is conspicuously small. He denies lues emphatically. The Wassermann blood test was twice negative. Spinal fluid also negative, cell count negative, Noguchi negative.

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[7] For details of the method of measuring the flow in the feet see Paper VII of this series.[6]

The blood-flow in the feet and hands was measured Dec. 18, 1912. There was no pain in left leg. Feet in bath at 2:04 p. m., in calorimeters at 2:17½ and out of calorimetrs at 2:59; 2,775 c.c. of water in each calorimeter. Pulse (sitting) 92. He felt the feathers equally well on both legs.

I was asked to make an examination of the flow in the feet in case some light might thus be thrown on the diagnosis. The flow in the right foot was 1.89 grams per 100 c.c. per minute and in the left 1.56 grams (for the last ten minutes in the calorimeters), with an average room temperature 23.9 C. From the small deficiency in the flow in the left foot as compared with the right, it was concluded that there was no obstruction in the main arterial supply of the left leg which could account for the slow healing of the sore and for the pain in the leg. If the cause was vascular it was therefore a vasomotor affair, possibly even a local vasoconstriction due to the pain itself. Undue susceptibility to vasoconstriction might account for the relatively small flow in both feet. The slow increase in the flow in the left foot at the beginning of the observations supports the view that it was peculiarly susceptible to vasoconstriction. The consequence of this stubborn vasoconstriction is that the ratio of the flow in the left foot to that in the right for a period of twenty-four minutes in the calorimeters, beginning seventeen and one-half minutes from the first insertion therein, is 1:1.55, while for the last ten minutes in the calorimeters it is 1:1.21. The cause of the small flow was not a central one (deficiency in the driving power of the heart), since the flow in the hands was normal (10.62 grams for the right hand per 100 c.c. per minute and 10 grams for the left with room temperature 23.6 C.).

Philip D., a street laborer, 47 year old, a dispensary patient. Weight 170 pounds; height 5 feet, 10½ inches. His right arm was shorter than the left from inflammatory rheumatism, he said, 13 years previously. Some arteriosclerosis. He had had pneumonia, pleurisy and rheumatism. He had a troublesome cough and coughed a good deal while his hands were in the calorimeters.

He had a great many clothes on but the hands were not warm. The blood-flow in the hands was examined Dec. 20, 1910. At 2:23 p. m. hands put in bath; at 2:32 in calorimeters, and at 2:45 taken out of calorimeters. He was in a hurry to get back to work and therefore his hands were left only nine minutes in the bath; 3.050 c.c. of water in each calorimeter. This was one of the earlier cases examined and the calorimeter and room temperature was 19.1 C. Bath temperatures were lower than are usually employed now.

TABLE 7.—Calorimeter Measurements in Case of Philip D.

Time	Right	Left	Time	Right	Left
2:30	29.49	29.44	2:40	29.50	29.50
2:33	29.40	29.38	2:41	29.53	29.61
2:34	29.41	29.38	2:42	29.59	29.60
2:35	29.40	29.38	2:43	29.61	29.63
2:36	29.41	29.40	2:44	29.66	29.70
2:37	29.41	29.40	2:45	29.69	29.70
2:38	29.43	29.42	2:55	29.54	29.56
2:39	29.47	29.45	....	.....	.....

Cooling of calorimeters in 10 minutes: R., 0.15 degrees; L., 0.14 degrees. Volume of right hand in calorimeter, 385 c.c., of left, 375 c.c. Pulse (standing) 68. Mouth temperature 37.0 C.

The flow in the right hand, which showed no wasting, was 7.05 grams per 100 c.c. per minute; in the left 7.41 grams, with the rather low room temperature of 19.1 C. These flows are fair for his age and clinical condition. As his haste to return to work did not permit a sufficiently long examination, and no opportunity to repeat the observations occurred, it is not possible to say whether the small deficiency in the right hand flow is permanent and associated with the shortening of the arm.

Some interesting cases in which obvious differences between the two hands exist were found in unilateral inflammations. Of these we shall cite three—one in which the inflammation was due to an infected finger, one in which it was due to gout, and a third in which it was due to a sprain.

Charles C., a teamster, aged 36, had an infection of the right hand, with considerable swelling and redness; otherwise he was in good health. The protocol has been already published.[8] The flow was 11.93 grams per 100 c.c. per minute, or allowing for the edema fluid, 13.05 grams in the right hand against 4.92 grams in the left, with room temperature at 23.8 C.

There can be no doubt that along with an increase in the flow in the inflamed hand in this case there goes a decrease in the flow in the normal hand, since 4.92 grams is an abnormally small flow for a healthy man of this age. The suggestion is that in order to provide for the increased flow in the infected area a vasoconstriction, possibly elicited reflexly through the pain nerves of the infected hand, is brought about

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8. Heart, 1911, iii. 82.

elsewhere and particularly in the symmetrically placed parts on the opposite side.

However this may be, a fact of interest emerges when the vasomotor reflexes from the left to the right hand are studied. Immersion of the left hand in cold water caused scarcely any reduction of the flow in the right hand (from 11.93 to 11.15 grams, or allowing for the edema liquid, from 13.05 grams to 12.20 grams). This is a very much smaller reaction than normal, and suggests that vasoconstrictor impulses to the inflamed part are blocked, perhaps, by a local action of the bacterial products or of something produced in the reaction between them and the leukocytes on the vasomotor nerve endings. It is clear that such a block may be of importance in maintaining against casual and vagrant vasoconstrictor impulses, so to say, the full stream of blood which is so important a factor in combating the infection.

Immersion of the left hand in warm water also caused hardly any increase in the flow through the right hand beyond promptly removing the small effect of the cold water. But this is of less significance, as the vasodilatation in the infected hand was probably already nearly maximum, and it is usual to obtain a relatively small reflex vasodilatation in a hand with a large initial flow. It is, however, again of interest that the initial vasoconstriction which normally follows immersion of the contralateral hand in warm water is here absent, a further indication of a block on the vasoconstrictor path. A different picture is presented by the case of gouty (non-bacterial) inflammation in which two examinations were obtained.

Harry S., aged 50, a patient at the City Hospital. He had suffered from gout for twenty years. He had no knowledge of its having been in the family before him. His mother suffered much from rheumatism. There are tophi in the scrotum as well as in the ears. There is a trace of albumin in the urine, also some fine granular and hyaline casts. First examination of the hand flow April 3, 1912. The right wrist and hand were painful and swollen. Hands in bath at 2:20 p. m., in calorimeters at 2:32 p. m. Mouth temperature 37.1 C. At 2:44 p. m. left hand put in water at 43 C.

Second examination of hand flow July 9, 1912. The right wrist and hand were much swollen and there was considerable pain. The day was warm and muggy. Pulse (sitting) 100. Hands in bath at 2.07 p. m.; in calorimeters at 2:17 p. m. Only 2,965 c.c. of water was put into each calorimeter on account of the swelling of the right hand. At 2:30 p. m. left hand put into water at 8.3 C. He feels it very cold.

At the first examination with room temperature 24.3 C., the flow was 6.88 grams per 100 c.c. of hand per minute (or allowing for the swelling, 7.47 grams) in the right hand and 3.07 grams in the left. Immersion of the left hand in warm water caused the usual initial diminution of the flow in the right to 4.66 grams (or, allowing for swelling, 5.06 grams), followed by an increase to 9.88 grams (or, allowing for the edema, 10.73 grams), a good vasodilatation. It must, of course, be remembered that the initial flow in the right hand did not correspond with anything like a maximal vasodilatation. It is therefore all the more significant that immersion of the left hand in cold water caused a marked and persistent decline of the flow in the right hand to 3.84 grams (or, allowing for the swelling, to 4.16 grams). There is, then, in this case of non-bacterial inflammation, no sign of vasoconstrictor block.

TABLE 8.—CALORIMETER MEASUREMENTS IN CASE OF HARRY S.

Time	Right	Left	Room Temp., C.	Time	Right	Notes
2:33	30.32	30.21	.....	2:51	31.11	At 2:51 left hand put in water at 8 C.
2:34	30.36	30.22	.....	2:52	31.13	
2:35	30.37	30.23	.....	2:53	31.18	
2:36	30.40	30.23	24.2	2:54	31.19	
2:37	30.43	30.23	.....	2:55	31.21	
2:38	30.49	30.24	.....	2:56	31.23	Room at 24.0 C.
2:39	30.55	30.27	.....	2:57	31.245	
2:40	30.59	30.305	24.3	2:58	31.27	
2:41	30.63	30.315	.....	2:59	31.29	At 2:59 left hand dried and wrapped.
2:42	30.69	30.33	.....	3:00	31.295	Room at 24.1 C.
2:43	30.71	30.33	.....	3:01	31.32	
2:44	30.76	30.34	.....	3:02	31.33	
2:45	30.795	.....	.....	3:03	31.37	
2:46	30.805	.....	24.5	3:04	31.395	
2:47	30.86	.....	.....	3:05	31.42	At 3:05 hand out of calorim. Room 32.7
2:48	30.92	.....	.....	3:13½	31.33	At 3.13½ L. is at 30.07 C.
2:49	30.99	.....	.....	....	.....	
2:50	31.06	.....	24.2	....	.....	

Cooling of calorimeters: R., 0.09 degree in 8½ minutes; L., 0.27 degree in 29½ minutes. Volume of right hand in calorimeter 456 c.c., of left hand 404 c.c. Pulse (sitting) 76. Water equivalent of calorimeters with contents, R., 3,460, L., 3,418.

The same fact comes out fully as well in the second examination, which was made on a very warm day with a room temperature of 29.7 C. The right hand was much more swollen at the second examination than at the first. At neither examination was there any pain in the left hand. The initial flow was 13.27 grams per 100 c.c. per minute (taking only the flow corrected for the edema liquid) in the right and 8.13 grams in the left hand. As compared with the previous examination, the flow in the left hand is, of course, proportionately more increased by the high external temperature than that in the right. It is still, however, for the temperature a distinctly subnormal flow. On immersion of the left hand in cold water, the flow in the right was diminished to 8.47 grams, a very fair reaction in the normal direction, and this was augmented to 12.82 grams, nearly the initial flow, on subsequent immersion of the left hand in warm water.

TABLE 9.—SECOND EXAMINATION IN CASE OF HARRY S.

Time	Right	Left	Room Temp., C.	Time	Right	Notes
2:16	31.39	31.30	29.7	2:34	32.535	The cold water does not feel as bad as it did.
2:18	31.47	31.42	.....	2:35	32.58	
2:19	31.55	31.445	.....	2:36	32.61	
2:20	31.625	31.48	.....	2:37	32.66	He says the cold water is now more tolerable.
2:21	31.70	31.525	29.65	2:38	32.69	
2:22	31.78	31.56	.....	2:39	32.74	At 2:39 left hand put in water at 42.8 C. Room 29.6 C.
2:23	31.87	31.625	.....	2:40	32.795	
2:24	31.94	31.66	.....	2:41	32.825	
2:25	32.03	31.73	29.8	2:42	32.89	
2:26	32.105	31.77	.....	2:43	32.955	Room 29.9 C.
2:27	32.18	31.82	.....	2:44	33.01	
2:28	32.24	31.855	.....	2:45	33.07	
2:29	32.32	31.90	.....	2:46	33.125	Room 30.0 C.
2:30	32.38	31.95	.....	2:47	33.195	
2:31	32.41	.....	.....	2:48	33.25	At 2:48 hand out of calorimeter.
2:32	32.47	.....	.....	3:02	33.16	At 3:02 temperature of L. is 31.825 C.
2:33	32.50	.....	29.7	....	.....	

Cooling of calorimeters: R., 0.09 degrees in fourteen minutes; L., 0.125 degrees in thirty-two minutes. Volume of right hand in calorimeters 530 c.c., of left hand 410 c.c. Rectal temperature 37.95. Water equivalent of calorimeters with contents: R., 3.519; L., 3,423. Blood-pressure left arm, systolic 114.5 (palpation), 114 (stethoscope), 85.5 (sound gone). Another observation with stethoscope, systolic 108, 88 (sound gone).

It would not be profitable to speculate on the reasons for the difference in the reflex vasomotor reactions in the two cases related further than to point out that the local infection is an acute affair, a bacterial invasion fraught with imminent peril to the organism if it be not promptly dealt with. The mechanism exists also, and in the blood, for the effective and rapid destruction of the bacteria. On the other hand, if the essential condition of the gouty paroxysm be the deposition of urates in the tissue, while an increase in the blood-stream, which does take place, may doubtless be of value in aiding the tissue to segregate the deposit so as to minimize its action as a mechanical irritant, no increase in the blood flow, however great and however sustained, will soon effect the re-solution of the deposit, which in any case is quite indifferent to the body as a whole and exposes it to no danger of invasion.

The third case was that of Martin B., a man aged 66 years, who had sprained the little finger of his left hand three days before the examination. The hand was swollen, but not greatly. He said the pain had diminished. The difference in flow between the two hands is very striking (1.7 grams per 100 c.c. per minute for the right hand and 5.2 grams for the left with a room temperature of 23.4 C.). Absolutely the flow is small in both hands, which is accounted for by the arteriosclerosis,[9] the renal disease and the age of the patient. It may be worth pointing out once more that the high systolic arterial pressure far from indicating a copious flow, is commonly the index of a high peripheral existence, coupled with a small flow. No observations were made on the vasomotor reflexes, although it would have been interesting to compare a case of traumatic non-bacterial inflammation with the case of infection (Charles C.). The complicating conditions, however, especially the arteriosclerosis, which tends to prevent marked vasomotor reflexes, rendered the case an unfavorable one for these tests. Yet there is little doubt that the small flow in the right hand is in part due to reflex vasomotor stimulation, probably from the other hand (pain stimulation?).

Martin B., a carpenter, aged 66, height 5 feet, 8 inches, weight 165 pounds, rather stout, born in Bavaria, but long in this country. Drinks considerable quantities of beer. He has been coming to the dispensary for some time. Extract from dispensary record Nov. 25, 1910: "Marked arteriosclerosis. Albumin in urine, also hyaline casts, epithelial cells, mucus and blood. No sugar. Puffiness under the eyes. Boundaries of heart dulness, upper border of third rib, right sternal margin, and 2½ fingers outside the left nipple. Emphysema." On Jan. 16, 1912, he fell and hurt his left hand, spraining the little finger. The left hand is swollen, but not greatly. He says the pain is better than it was. The blood-flow in the hands was measured Jan. 19, 1911. Systolic blood-pressure 151. Hands put into bath at 2:58 p. m., into calorimeters at 3:10 p. m., and out of calorimeters at 3:24; 3,050 c.c. of water in each calorimeter. Mouth temperature 37.38 C.; room 23.2 C.

TABLE 10.—Calorimeter Measurements in Case of Martin B.

Time	Right	Left	Time	Right	Left
3:09	29.49	29.33	3:19	29.49	29.60
3:12	29.45	29.33	3:20	29.50	29.66
3:13	29.45	29.38	3:21	29.50	29.69
3:14	29.46	29.41	3:22	29.52	29.74
3:15	29.46	29.45	3:23	29.53	29.79
3:16	29.47	29.49	3:24	29.54	29.84
3:17	29.48	29.52	3:42	29.38	29.67
3:18	29.48	29.57	....	.....	.....

Cooling of calorimeters in 18 minutes: R., 0.16 degrees; L., 0.17 degrees. Volume of right hand 490 c.c., of left hand 497 c.c. He is right handed. Water equivalent of calorimeters with contents, R., 3,522, L., 3,528. Room temp., 23.6 C.

The influence of pain in diminishing the flow in the hands when the inflamed area is not situated in the hands themselves, is perhaps illustrated in the case of George S.

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[9] See Paper XI (unpublished) of this series, The Archives Int. Med., 1914.

George S., a teamster, aged 37 years, was admitted at the dispensary Jan. 31, 1911, suffering from an inflamed right elbow (acute articular rheumatism). He first felt pain in the elbow three weeks previous to admission suddenly while he was sitting in a saloon. The swelling came on afterwards. He had no knowledge of any injury. The elbow on admission was hot and swollen. He had used alcohol and tobacco to excess. He had delirium tremens in July, 1910. He had chancre four years previously, but denied gonorrhea. He had swelling of four toes of left foot for three days four months previously. The heart was normal. On February 2 the arm was not quite so red, and on February 6 it was much better. The hand and forearm were quite unaffected. His height was 5 feet, 7 inches; weight 156 pounds.

The flow in the hands was examined Feb. 2, 1911. The day was cold and he had no gloves on when he came to the dispensary. Pulse (sitting) 92. Hands in bath at 2:40 p. m., in calorimeters at 2:50 and out of calorimeters at 3:06. The experiment was shorter than had been intended as he said he was suffering so much pain that he could not keep the right hand in any longer. There was 3,050 c.c. of water in each calorimeter.

TABLE 11.—CALORIMETER EXAMINATION IN CASE OF GEORGE S.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
2:49	29.74	29.79	.....	3:00	29.75	29.76	22.3
2:51	29.69	29.73	.....	3:01	29.77	29.80	.....
2:53	29.69	29.73	22.2	3:02	29.79	29.80	.....
2:54	29.70	29.74	.....	3:03	29.80	29.81	.....
2:55	29.69	29.73	.....	3:04	29.82	29.83	22.3
2:56	29.70	29.74	.....	3:05	29.83	29.83	.....
2:57	29.71	29.74	.....	3:06	29.85	29.86	.....
2:58	29.72	29.74	.....	3:17	29.72	29.73	22.2
2:59	29.73	29.74	.....	....	.....	.....	.....

Cooling of calorimeters in eleven minutes; 0.13 degrees for R. and L. Mouth temperature 37.05 C. Volume of right hand in calorimeter, 487 c.c., of left hand 456 c.c. Water equivalent of calorimeters with contents, R., 3,520; L., 3,495.

As was to be expected from the fact that the inflammation, although unilateral, does not involve either hand, the blood-flow is approximately the same in the two hands (3.18 grams per 100 c.c. per minute for the right hand and 3.40 grams for the left hand, with room temperature 22.2 C.). So far as it goes the deficiency in the right hand as compared with the left, if the markedly subnormal flow for the age of the patient is determined in any important degree by reflex impulses from the inflamed area, may be due to the closer anatomical connection of the afferent paths from the right elbow with the efferent paths to the right than with those to the left hand. Another factor which probably contributed to the small flow is that the man came to the dispensary on a cold day without gloves and could not be kept for a sufficiently long interval before the examination. Also he was a teamster, accustomed to the exposure of the hands to cold, and there is some evidence that these "cold-adapted" hands require an unusually long time to respond to our standard conditions of temperature.

It may be instructive to cite here a case in which one hand remained persistently swollen without any symptoms or history of inflammation.

Miss M. F., 34 years of age, 5 feet, 2 inches in height, a cook in a restaurant, was seen at the dispensary Feb. 16, 1911, on which day the blood-flow in the hands was measured. The left hand was permanently swollen to a moderate degree. The swelling came on about two years previously and had not varied to any extent. There was no pain or discomfort and no loss of power, but she felt the left hand to be colder than the right, especially in summer. There was a transverse scar on the radial side of the back of the wrist which she said was due to the lancing of a boil about the time the swelling came on. She did not connect the lancing of the boil with the swelling, to which, indeed, she paid no attention, coming to the dispensary not on her own account, but with a friend. Nevertheless on cross-examination she said she felt pretty sure that there was no swelling until after the boil had been lanced. On the day of examination both hands felt rather cold, and to the touch there was no difference between them. Pulse 110 (sitting). Hands in bath at 3:53 p. m., in calorimeters at 4:04 and out of calorimeters at 4:23. Mouth temperature 37.02 C.

TABLE 12.—Calorimeter Measurements in Case of Miss F.

Time	Right	Left	Room Temp., C.	Time	Right	Left	
4:03	29.96	29.50	.....	4:15	30.11	29.71	.....
4:05	29.95	29.50	.....	4:16	30.12	29.72	.....
4:06	29.96	29.50	23.9	4:17	30.13	29.75	.....
4:07	29.96	29.52	.....	4:18	30.18	29.81	.....
4:08	29.97	29.53	.....	4:19	30.19	29.83	.....
4:09	29.99	29.56	.....	4:20	30.22	29.85	.....
4:10	30.01	29.60	.....	4:21	30.25	29.88	.....
4:11	30.04	29.62	.....	4:22	30.28	29.90	.....
4:12	30.06	29.65	.....	4:23	30.29	29.91	.....
4:13	30.07	29.68	.....	4:40	30.11	29.73	.....
4:14	30.09	29.70	24.1	....	.....	.....	.....

Cooling of calorimeters in seventeen minutes, 0.18 degrees for R. and L. Volume of right hand in calorimeter, 355 c.c., of left hand 380 c.c.

The flow in the right hand comes out 4.81 grams per 100 c.c. per minute, in the left 4.78 grams (or, allowing for the probable amount of edema liquid, 5.4 grams), with room temperature at 24 C. The contrast with the cases of inflammation is striking. The flow in the affected hand is somewhat more copious than in the other, indicating that the cause of the edema is probably not obstruction to the venous return. In view of the coincidence between the appearance of the edema and the opening of the boil, it seems most natural to connect the swelling with injury to the radial nerve not as yet recovered from, since there is no indication of any infection of the lymphatics at that time. It is true that Simons[10] has stated that the radial nerve does not carry vasomotor fibers to the hand. But even if this be the case, and the evidence is by no means conclusive, this does not preclude the production of permanent vasomotor effects through an injury to a nerve. Infection of the nerve path at the seat of injury, as might occur if the nerve were divided through the boil, might delay regeneration. Thrombosis of veins or lymphatics might also be thought of, but with the free anastomosis it is difficult to see how this could cause permanent edema. The fact that it was in summer that she felt the left hand cold in comparison with the right indicates that the vasomotor response to external heat is less perfect than in the normal hand. A case of edema in the foot and leg probably connected with a traumatic injury will be referred to in another connection (Paper XI of this series, case of Charles H.).

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[10] Simons: Arch. f. Physiol., 1910, p. 559.

In this connection may be mentioned experiments in which the flow was tested in a normal man (M. C.) after bandaging one hand so as to cause temporary anemia of the part, or after bandaging one forearm so as to cause temporary congestion of the hand. In both cases the bandage was removed just before the hands were put into the calorimeters.

M. C., a normal man 22 years old, height 5 feet, 10 inches, weight 146 pounds (stripped). April 17, 1911, an experiment was conducted to test the effect of bandaging the hand on the blood-flow after removal of the bandage. At 3:38 p. m. began bandaging the left hand from the finger tips upward with a rubber bandage (Martin's). Bandaging was completed at 3:39½ p. m., at which time both hands were immersed in the bath, the temperature of which was 30.2 C. At 3:50 p. m. the hands were put into the calorimeters, the bandage having been rapidly removed from the left hand while it was still kept in the bath. At 4:04 p. m. the hands were removed from the calorimeters. Volume of right hand in calorimeter 473 c.c., of left hand 448 c.c. Rectal temperature 36.9 C.

TABLE 13.—Calorimeter Measurements in a Normal Individual After the Hands Had Been Bandaged

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
3:48	29.99	30.04	23.8	3:59	30.31	30.44	24.4
3:51	30.02	30.08	.....	4:00	30.37	30.50	.....
3:52	30.06	30.15	.....	4:01	30.41	30.54	24.4
3:53	30.09	30.21	24.4	4:02	30.45	30.59	.....
3:54	30.12	30.23	.....	4:03	30.49	30.61	24.4
3:55	30.16	30.28	.....	4:04	30.52	30.64	.....
3:56	30.19	30.32	.....	4:04½	30.52	30.64	.....
3:57	30.22	30.35	.....	4:10½	30.47	30.60	24.2
3:58	30.28	30.41	.....	....	.....	.....	.....

Here the flow per 100 c.c. per minute in the right hand works out at 6.25 grams and in the left hand at 7.04 grams for thirteen minutes in calorimeters. For the first 11 minutes of this period the calculated flows are 6.26 grams per 100 c.c. per minute for the right hand and 7.45 grams for the left. The flow in the previously anemic hand is therefore increased to a moderate degree. Probably the increase is somewhat greater than it appears to be from these figures, since the flow per 100 c.c. per minute in M. C. is nearly always somewhat less for the left than for the right hand. In both hands the flow is less than usual for this man, as the hands had been long used for blood-flow observations on the same afternoon, and this causes vasoconstriction.

M. C., May 4, 1911. Experiment on the effect of bandaging the forearm on the flow in the hand after removal of the bandage. The left forearm was bandaged from above downward with a Martin's bandage. The bandaging was begun immediately below the bend of the elbow and carried down nearly to the upper pencil mark on the wrist, the arm being all the time in the dependent position. The hand was well filled with blood before the application of the bandage was begun and the bandage was tight enough to retain the venous blood without greatly affecting the arterial flow.

At 2:37 p. m. the hands were put into the bath and at 2:47 into the calorimeters, the bandage having been rapidly removed from the left forearm just before the hands were taken out of the bath. The hands were taken out of the calorimeters at 3:06 p. m. Pulse (sitting) 90. Cooling of calorimeters in nine minutes: R., 0.115 degrees; L., 0.11 degrees. Volume of right hand in calorimeter 486 c.c., of left 470 c.c. Water equivalent of calorimeters with contents, R., 3,484, L., 3,471. Rectal temperature 37.2 C.

TABLE 14.—Calorimeter Measurements After Bandaging the Forearm

Time	Right	Left	Notes
2:45½	29.54	29.63	
2:48	29.61	29.66	He feels left hand warmer than right.
2:49	29.72	29.75	
2:50	29.81	29.84	
2:51	29.90	29.92	Right hand feels water cool when stirred, but not left. Left feels tired.
2:52	29.99	29.98	
2:53	30.11	30.07	Room 23.3.
2:54	30.17	30.13	
2:55	30.29	30.25	Left still feels warmer than right.
2:56	30.41	30.34	
2:57	30.47	30.40	Left feels water only when stirring is begun.
2:58	30.58	30.47	Room 23.2.
2:59	30.67	30.54	
3:00	30.74	30.61	Left now feels water cool the whole time of stirring like right, but not as distinctly as right.
3:01	30.83	30.69	
3:02	30.93	30.76	Now feels no difference in warmth of the two hands, but left still a little tired.
3:03	31.01	30.83	
3:04	31.09	30.90	Room 23.2.
3:05	31.17	30.94	
3:06	31.235	31.01	The hands now feel the same.
3:15	31.12	30.90	Room 22.8.

For the first nine minutes in the calorimeters the flow comes out 12.86 grams per 100 c.c. per minute for the right hand, and 11.61 grams for the left. For the second nine minutes the flows are 13.31 grams, and 10.96 grams for the right and left hands, respectively; for the whole eighteen minutes, 13.12 grams and 11.26 grams. The disproportion between the flows in the two hands cannot be due to the deeper parts of the left hand having more nearly acquired the temperature of the bath owing to the impeded circulation and being then heated up by the blood during the first part of the period of immersion in the calorimeters. For the disproportion is greater in the second than in the first nine minutes. The combined flow in the two hands remains practically constant throughout.

In the experiment of May 24, 1911, on the same man, the effect of moderate compression of the veins by a rubber band kept on one forearm during the observations is illustrated. Although the diminution in the flow is distinct, it is far less than might have been expected from the swelling of the veins in the hands. The reason is that the venous pressure quickly rises to the point at which blood again passes freely heart-wards under the band. Evidence will be brought forward in the next paper (Paper X) that some degree of venous engorgement in certain cardiac lesions in which the beat of the heart is still strong and orderly, the myocardium not having seriously deteriorated, may even be associated with an increased hand flow, the rise of venous pressure, which is general, not local as in the experiment under discussion, being more than compensated by the concomitant rise in the arterial pressure and the widening of the vascular path.

M. C., May 24, 1911. Pulse (sitting) 87. Hands in bath at 2:29 p. m., in calorimeters at 2:39½, out of calorimeters at 3:10. Mouth temperature 36.7 C. At 2:48½ put band on right forearm about 8 cm. above the upper mark. The band was made of rubber tubing. It compressed the veins without affecting the radial pulse so far as could be felt by the finger. After it was put on the subject said his right hand felt "heavy," and later on had a kind of burning sensation. Band taken off at 3:00½ p. m. Cooling of calorimeters: R., 0.95 degrees in 9 minutes; L., 0.10 degrees in nine and one-half minutes. Volume of right hand in calorimeter, 470 c.c.; of left hand, 457 c.c. Rectal temperature 37.3 C.

For five minutes before the application of the band the flow works out at 17.98 grams per 100 c.c. per minute for the right hand, and 16.65 grams for the left, with the high room temperature of 26.9 C. For the first five minutes with the band on the right arm the flows were, respectively, 15.55 grams per 100 c.c. per minute for the right, and 15.82 grams for the left hand. For the last six minutes of application of the band the flows were 13.56 grams and 13.93 grams for the right and left hands, respectively. The original preponderance of flow in the right hand has therefore been changed by the obstruction to the venous return from the right hand to a preponderance in favor of the left. That this is not due to some accidental (vasomotor?) effect in the course of the experiment is shown by the restoration of the preponderance of the right hand when the band is removed, the flow for nine minutes coming out at 15.20 grams per 100 c.c. per minute for the right, and 14.84 grams for the left hand.

The changes in the flow in the left hand suggest that the interference with the flow in the right (local asphyxia) may have caused some compensatory vasoconstriction elsewhere, especially in the left hand, as a means of raising the arterial pressure and thus helping to overcome the obstruction.

TABLE 15.—Calorimeter Measurements with Rubber Band on Arm

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
2:39	30.29	30.33	.....	2:57	32.065	32.03	.....
2:41	30.48	30.51	26.5	2:58	32.11	32.10	26.4
2:42	30.62	30.64	.....	2:59	32.20	32.16	.....
2:43	30.76	30.78	27.1	3:00	32.26	32.225	.....
2:44	30.88	30.90	26.9	3:01	32.30	32.295	26.8
2:45	31.02	31.02	.....	3:02	32.37	32.335	.....
2:46	31.125	31.105	26.6	3:03	32.43	32.405	.....
2:47	31.22	31.205	.....	3:04	32.495	32.46	.....
2:48	31.34	31.30	.....	3:05	32.58	32.535	26.5
2:49	31.41	31.37	.....	3:06	32.65	32.61	.....
2:50	31.505	31.45	.....	3:07	32.72	32.68	.....
2:51	31.595	31.535	.....	3:08	32.785	32.735	26.9
2:52	31.68	31.63	.....	3:09	32.85	32.81	.....
2:53	31.775	31.73	26.6	3:10	32.905	32.87	.....
2:54	31.85	31,81	.....	3:19	32.81	.....	.....
2:55	31.92	31.89	.....	3:19½	.....	32.77	26.5
2:56	31.995	31.95	.....	....	.....	.....	.....

Certain cases in which congenital or at least very long standing anatomical defects existed in one hand without markedly affecting its functional power were examined. Here, as was to be expected, no great difference in the flow per 100 c.c. of hand was made out.

Helen P., a girl 21 years old, height 4 feet 11 inches, well nourished. She works with a sewing machine in a factory. She said she had rheumatism at 6 months, and St. Vitus' dance two years previous to examination. She came to the dispensary for "nervousness." She has no symptoms of chorea, but is afraid she is going to have it again. Menstruation is disturbed, her period falling too late for the past two or three months, but there is no more than the usual amount of discomfort and the discharge is not altered in quantity. She has suffered much from headache the past two or three months. Her left wrist is deformed (subluxation anteriorly), the styloid process of the ulna being very prominent. The left hand is considerably smaller and the left ulna and radius shorter than the right. This has been true for a long time, perhaps from birth. The left hand is normally formed and she uses it in all ways in which a normal hand would be used, only it is not so strong as the right hand. The left anterior limb is shorter than the right and the girth of the forearm is distinctly less to the eye. The left hand does not get cold any more than the right and does not require to be better protected in winter. The pulse at the wrist is of fair volume to the finger. The blood-flow was examined July 20, 1911, the first day she came to the dispensary. Pulse (sitting) 88. Hands in bath at 2:21 p. m., in calorimeters at 2:45⅓ p. m. The lower mark on the left wrist had to be drawn through the middle instead of at the lower border of the styloid process of the ulna, as the hand was bent somewhat to the side, and the whole hand could not otherwise have been included in the calorimeter. Mouth temperature 37.6 C.

With the rather high room temperature of 26 C. the flow in the right hand was 9.08 grams per 100 c.c. of hand per minute, in the left 8.81 grams. The vasomotor reflexes from the right to the left hand were less marked than those normally observed, but in the normal direction.

TABLE 16.—CALORIMETER MEASUREMENTS IN CASE OF HELEN P.

Time	Right	Left	Notes
2:45	30.495	30.45	
2:47	30.575	30.47	
2:48	30.60	30.51	
2:49	30.64	30.54	Room 26.0 C.
2:50	30.69	30.60	
2:51	30.73	30.63	
2:52	30.775	30.65	
2:53	30.80	30.69	
2:54	30.85	30.72	
2:55	30.89	30.74	Room 26.2 C.
2:56	30.92	30.765	At 2:56 put right hand in water at 8.3 C.
2:57	.....	30.80	
2:58	.....	30.825	She feels it very cold and complains of it.
2:59	.....	30.835	Still complains of the cold water, though it is now more tolerable.
3:00	.....	30.87	
3:01		30.89	
3:02		30.93	
3:03		30.96	
3:04		30.97	At 3:04 put right hand in water at 43 C.
3:05		30.99	
3:06		31.005	Room 26.2 C.
3:07		31.025	
3:08		31.04	
3:09		31.08	
3:10		31.11	
3:11		31.135	Room 26.1 C.
3:12		31.155	At 3:12 hand out of calorimeters.
3:17		31.12	At 3:17 right is at 30.77 C.

Cooling of calorimeters: R., 0.15 degrees in twenty-one minutes; L., 0.035 degrees in five minutes. Volume of right hand, 282 c.c., of left hand, 230 c.c.

Max H., aged 46, with spastic paralysis of the left wrist (birth palsy), showed a flow in the left hand but little less than that in the right (right hand 10.71 grams per 100 c.c. per minute, left hand 10.2 grams with room temperature 20.5 C.). These flows are perfectly normal. He uses the left hand largely in his work, that of a telegraph operator. It was obviously well supplied with blood. The protocol of the case has already been published.[10]

Marie G., 15 years old, congenitally deficient in intellect and brought on this account to the dispensary by her mother, July 20, 1911. She became violent at times and would bite her mother. On admission she was in good humor. She could read books and newspapers and did so regularly. She played the piano and easily picked up a melody which she heard. She could also write, but she was quite defective in certain points; for example, she did not understand the

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[10] Proc. Soc. Exper. Biol. and Med., 1910, viii, 43.

time of day. She did not walk until she was 3 years old. She had menstruated regularly for about two years prior to being seen. Her left hand was congenitally defective, the thumb being wanting; otherwise it was perfectly formed, though small. The left arm both upper and lower, was much smaller in girth than the right, and the elbow joint appeared very prominent between the two ill-developed segments. The left hand easily became cold in winter. She used it quite freely, but not so much as the right. The whole left anterior extremity was somewhat shorter than the right. The mother said the child's left leg was also affected to some extent, but this was not now noticeable in her walk. She was well grown and looked well nourished. The blood-flow in the hands was examined July 20, 1911. Hands in bath at 3:24 p. m., in calorimeters at 3:26. Mouth temperature 37.35 C. At 3:50 p. m. right hand put into water at 42.8 C. Cooling of calorimeters: R., 0.12 degrees in twenty-two minutes; L., 0.14 degrees in nineteen minutes. Pulse (sitting) 88. Volume of right hand in calorimeter, 260 c.c.; of left hand, 170 c.c.

TABLE 17.—Calorimetric Measurements of Marie G.

Time	Right	Left	Room Temp., C.	Time	Left	Notes
3:35¼	30.13	30.20	.....	3:56	30.435	
3:37	30.12	30.17	26.2	3:57	30.47	
3:38	30.125	30.17	.....	3:58	30.50	
3:39	30.145	30.19	.....	3:59	30.525	
3:40	30.16	30.18	.....	4:00	30.535	
3:41	30.185	30.21	.....	4:01	30.54	
3:42	30.20	30.22	26.5	4:02	30.56	
3:43	30.225	30.23	.....	4:03	30.565	At 4:03 right hand put in water at 13 C. She says she feels it very cold.
3:44	30.25	30.23	.....	4:04	30.59	
3:45	30.28	30.24	.....	4:05	30.60	Room at 26.3 C.
3:47	30.31	30.265	.....	4:06	30.61	
3:48	30.335	30.30	.....	4:07	30.62	
3:49	30.38	30.325	.....	4:08	30.625	
3:50	30.40	30.335	.....	4:09	30.635	
3:51	.....	30.35	26.25	4:10	30.64	
3:52	.....	30.355	.....	4:11	30.65	Hand removed from calorimeter at 4:11.
3:53	.....	30.36	.....	4:12	.....	Temp. of R. at 4:12, 30.28.
3:54	.....	30.38	.....	4:30	30.51	
3:55	.....	30.41	.....	....	.....	

With average room temperature 26.3 C. the flow in the right hand was 5.96 grams per 100 c.c. per minute, and in the left 6.6 grams per 100 c.c. per minute. The flow in the defective hand is thus somewhat greater than in the normal one, in contrast to the condition in a case of infantile paralysis in N. M., a boy 9½ years old, whose left hand was much atrophied and functionally of little use. In his right hand the flow was 15.0 grams per 100 c.c. of hand per minute against 7.6 grams in the left hand with room temperature 23.4 C. The protocol of N. M. has already been published.[10]

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It has been mentioned in a previous paper[11] that the flow in the distal half of the hand is greater than in the hand as a whole, doubtless because of the greater proportion of skin in the former. A case (John B.) in which some of the fingers of the left hand had been amputated, gave the opportunity of comparing two hands, one of which had suffered a considerable loss in its distal half. The blood-flow for the last ten minutes in the calorimeters was 7.20 grams per 100 c.c. per minute for the right and 5.34 grams for the left hand, a considerable deficiency in the hand which had lost fingers. The fact that the man had a right-sided pleurisy with effusion probably does not interfere with this conclusion, but, if anything, strengthens it. For it will be shown in a subsequent paper that this condition is usually associated with a diminished hand flow on the side of the lesion and that the difference may persist after the fluid has been removed.

John B., a longshoreman aged 51, admitted to City Hospital April 28, 1913, suffering from pulmonary tuberculosis, and pleurisy with effusion on the right side. He had a severe cold in the winter and in a short time the visiting nurse said he had tuberculosis. He was a well developed, well nourished man, weighing about 185 pounds, height about 5 feet, 11 inches. No cyanosis. Dyspnea present with physical signs of liquid in right pleural cavity. The heart presents nothing abnormal. Pulse full and regular. The sputum contains tubercle bacilli. May 4, at 4 p. m., 1,500 c.c. of straw-colored fluid was removed from the right thorax. Maximum temperature following admission 100.4 F. at 4 p. m., May 5. The whole middle finger and the second and third phalanges of the index finger of the left hand had been amputated for an injury. The blood-flow in the hands was measured May 6, 1913. Pulse (sitting) 100. Hands in bath at 2:46 p. m., in calorimeters at 2:57 and out of calorimeters at 3:15 p. m.

TABLE 18.—CALORIMETER MEASUREMENTS IN CASE OF JOHN B.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
2:56½	31.32	31.27	.....	3:07	31.68	31.455	.....
2:58	31.315	31.25	24.3	3:08	31.72	31.485	.....
2:59	31.33	31.265	.....	3:09	31.78	31.51	.....
3:00	31.37	31.28	.....	3:10	31.81	31.54	24.6
3:01	31.40	31.29	24.4	3:11	31.86	31.56	.....
3:02	31.43	31.315	.....	3:12	31.90	31.59	.....
3:03	31.47	31.34	24.35	3:13	31.94	31.64	24.7
3:04	31.52	31.36	.....	3:14	32.01	31.67	.....
3:05	31.57	31.39	.....	3:15	32.06	31.72	.....
3:06	31.62	31.44	24.2	3:32	31.84	31.53	.....

Cooling of calorimeters in seventeen minutes: R., 0.22 degrees; L., 0.19 degrees. Volume of right hand in calorimeter, 564 c.c., of left hand, 515 c.c. Rectal temperature 38.32 C. Water equivalent of calorimeters and contents, R., 3.546; L., 3,507. Blood-pressure, left arm, systolic 106; 93 (sound began to diminish but not suddenly); 77 (sound gone).

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[11] Heart, 1911, iii, 40.

The last case to be mentioned is that of Mrs. K., a woman 68 years old in whom Dr. Carl A. Hamann had ligated the innominate and right common carotid arteries for aneurysm of the subclavian.

Mrs. K., aged 68. The innominate and right common carotid arteries were tied at Charity Hospital by Dr. Carl Hamann on Feb. 26, 1913, for aneurysm of the subclavian artery. Wiring of the sac had previously been tried without effect. March 20, 1913, the blood-flow was compared in the two hands. No pulse could be felt in the right wrist or over the right brachial. She said the right hand got cold if left uncovered with bed-clothes. When hung down the veins filled well, as well as in the left hand. She said she felt the blood going down into the right hand when she hung it down. On being emptied by stripping, the veins on the back of the right hand filled from below slowly. The right hand could execute all movements, but was weak. She spoke of the loss of power in it. There was some paresthesia (pins and needles and numbness) in the right hand, but this she had before the operation, and it had not been intensified since. The nails on the right hand were getting clubbed. She noticed that they were getting "like those of a man." The change in the nails was present before the operation, but was now more marked. First examination of the blood-flow in the hands March 20, 1913. Hands in bath at 1:50½ p. m., in calorimeters at 2:00 and out of calorimeters at 2:13. Mouth temperature 37.0.

TABLE 19.—CALORIMETRIC MEASUREMENTS IN CASE OF MRS. K.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
1:59	30.78	30.65	26.2	2:08	30.675	30.70	.....
2:02	30.68	30.62	.....	2:09	30.67	30.72	26.7
2:03	30.675	30.64	26.5	2:10	30.67	30.75	.....
2:04	30.67	30.65	.....	2:11	30.675	30.78	.....
2:05	30.67	30.66	.....	2:12	30.675	30.795	.....
2:06	30.67	30.67	26.7	2:13	30.685	30.82	.....
2:07	30.675	30.69	.....	2:23	30.62	30.74	.....

Cooling of calorimeters in ten minutes: R., 0.07 degrees; L., 0.08 degrees. Volume of right hand, 378 c.c.; of left hand 360 c.c. Repeated the volume measurement with the same results. The right hand was not swollen. Pulse (sitting) 124. Water equivalent of calorimeters with contents, R., 3,397; L., 3,383.

Second examination March 21, 1913. The weather was decidedly colder than on the previous day. Pulse (sitting) 100. Mouth temperature 36.5 C. Hands in bath at 2:52 p. m.; in calorimeters at 3:02 p. m., and out of calorimeters at 3:25 p. m. At 3:18 the left hand was put into water at 43 C.

The blood-flows at the first examination work out at 1.50 grams per 100 c.c. of hand per minute for the right hand and 5.32 grams for the left hand (for the last five minutes in the calorimeters) with room temperature 26.7 C. The ratio between the flows in the two hands is 1:3.54. At the second examination the flow was 1.83 grams per 100 c.c. per minute in the right hand, and 6.38 grams in the left, with room temperature 22.7 C., the ratio being 1:3.48, almost identically the same ratio as at the first examination. The increased flow in both hands is therefore due to a central cause (better heart action, with a slower pulse?). Immersion of the left hand in warm water caused practically no change in the flow in the right. It is obvious that vasodilatation in the right hand could not be expected to materially affect the flow through the narrow and difficult collateral path. The block does not lie in the peripheral portions of the vascular path and cannot be removed by dilatation of peripheral areas.

TABLE 20.—SECOND CALOMETRIC TEST IN CASE OF MRS. K.

Time	Right	Left	Room Temp., C.	Time	Right	Left	Room Temp., C.
3:01	31.00	30.99	.....	3:15	30.925	31.08	22.7
3:03	30.93	30.92	22.7	3:16	30.92	31.10	.....
3:04	30.93	30.92	.....	3:17	30.925	31.125	22.7
3:05	30.93	30.925	22.7	3:18	30.925	31.15	.....
3:06	30.93	30.925	.....	3:19	30.93	.....	22.9
3:07	30.93	30.935	22.75	3:20	30.93	.....	.....
3:08	30.93	30.95	.....	3:21	30.93	.....	22.85
3:09	30.93	30.97	22.75	3:22	30.93	.....	.....
3:10	30.93	30.985	.....	3:23	30.925	.....	22.9
3:11	30.925	30.995	22.7	3:24	30.925	.....	.....
3:12	30.925	31.01	.....	3:25	30.925	.....	22.8
3:13	30.925	31.03	22.6	3:40	30.77	30.89	.....
3:14	30.925	31.06	.....	....	.....	.....	.....

Cooling of calorimeters: R., 0.155 degrees in fifteen minutes; L., 0.26 degrees in twenty-two minutes. Volume of right hand in calorimeter 369 c.c., of left hand 342 c.c. Water equivalent of calorimeters and contents, R., 3.390; L., 3,369. Blood-pressure in left arm, systolic 136; 69 (sound gone).

July 9, 1913, a third blood-flow examination was made. The patient was much improved and was doing all her own housework. The grip of the right hand was fair, though weaker than the left. She had gained considerably in weight and her arms and hands were distinctly more plump. There was no pulse in the radial. The veins on the back of the hand filled from below when emptied and much more quickly than at the last examination. She suffered a good deal from pain in the arm and shoulder. A report from Dr. Hamann, who saw her on June 24, 1913, is as follows:

"It is altogether likely that there is pressure on the brachial plexus by the end of the clavicle (a portion of the clavicle was resected at the operation), the new formed bone (which can be distinctly felt) and the cicatrix, and removal of more of the clavicle would most likely cure or relieve her. The aneurismal sac has been consolidated and but little trace of it can be felt. There is no evidence of any intrathoracic aneurism."

The results of the third blood-flow examination are entirely favorable to this view, for they show that any disability in the right hand was not now due to deficient circulation, and that the surgeon need not be deterred from operating, if an operation seemed desirable, by the fear that the symptoms might be dependent on a poor blood-flow.

TABLE 21.—SUMMARY OF

Case	Age	Date	Pulse-Rate	Blood-Pressure	Temperature of				Volume of Part in c.c.	
					Room	Art. Blood	Calorimeters		Right	Left
							Right	Left		
Steve S.	21	4/ 5/12	80	......	25.0	36.8	30.14	30.06	328	340
					24.8	.....	30.59	.....	....	....
					24.8	.....	30.86	.....	....	....
Frank P. ...	42	8/ 1/12	96	114.80	23.2	37.45	30.44	30.40	476	476
Charles B....	47	11/27/12	108	155.95	22.3	36.75	30.71	30.73	478	477
		11/29/12	98	......	22.5	36.3	31.33	31.48	1,313	1,313
					23.0	36.4	30.82	30.78	480	462
Charles W..	42	12/18/12	92	......	23.9	37.3	31.52	31.01	1,203	1,103
					23.6	37.4	31.61	31.57	2,422	2,221
Philip D....	47	12/20/10	68	......	19.1	37.0	29.56	29.56	1,272	1,303
Charles C...	36	2/27/11	116	......	23.8	37.8	30.59	29.87	580	500
					23.6	.....	37.42	.....	.....	....
					23.6	.....	31.97	.....	....	....
Harry S....	50	4/ 3/12	......	......	24.3	37.1	30.57	30.29	456	404
					24.5	.....	30.78	.....	....	....
					24.3	.....	30.96	.....	....	....
					24.1	.....	31.12	.....	....	....
					24.0	.....	31.24	.....	.....	....
		7/ 9/12	100	111.86	29.7	37.45	31.97	31.70	530	410
					29.7	.....	32.56	.....	....	....
					29.8	.....	33.00	.....	....	....
Martin B...	66	1/19/11	......	151.0	23.2	37.38	29.50	29.59	490	497
George S. ...	37	2/ 2/11	92	......	22.2	37.05	29.78	29.80	487	456
Miss M. F...	34	2/16/11	110	......	24.0	37.0	30.13	29.72	355	380
M. C.	22	4/17/11	......	......	24.4	36.4	30.27	30.36	473	448
		5/ 8/11	......	......	23.3	36.7	30.04	30.03	486	470
					23.2	.....	30.85	30.71	....	....
		5/24/11	......	......	26.9	36.8	31.05	31.04	470	457
					26.6	.....	31.63	31.59	....	....
					26.5	.....	32.06	32.02	....	....
					26.7	.....	32.60	32.58	....	....
Helen P. ...	21	7/20/11	88	......	26.0	37.6	30.76	30.64	282	230
					26.1	.....	.....	30.87	....	....
					26.1	.....	.....	31.06	....	....
Marie G. ...	15	7/20/11	88	......	26.3	37.3	30.28	30.26	260	170
					26.3	.....	.....	30.45	....	....
					26.3	.....	.....	30.6	....	....
John B. ...	51	5/ 6/13	100	106(93)77	24.4	37.8	31.82	31.56	564	515
Mrs. K.	68	3/20/13	124	......	26.7	37.0	30.68	30.74	378	360
		3/21/13	100	136.69	26.6	.....	30.68	30.72	....	....
		7/ 9/13	104	......	22.7	36.5	30.93	31.05	369	342
					26.2	37.0	31.89	32.03	424	385
					26.2	.....	32.39	.....	....	....
					26.4	.....	32.50	.....	....	....

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* Allowing 300 c.c. for edema fluid in each foot the flow would be 3.04 for the right and 3.24

† Allowing for the probable amount of edema fluid these flows would be 13.05, 12.20. and

‡ Allowing for edema fluid these flows would be 7.47, 5.06, 10.73, 6.90, and 4.16.

§ Allowing for edema fluid these flows would be 13.27, 8.47, and 12.82.

¶ Allowing for edema fluid, 5.4.

Heat Given Off in Gram-Calories			Blood-Flow in Gm. Per Min.		Flow per 100 c.c. of Part per Min.		Notes
Right	Left	In Min.	Right	Left	Right	Left	
1,242	1,010	9	23.09	18.50	7.04	5.44	Burned hands; right worse.
2,283	....	12	34.04	.....	10.38	.....	Left hand in water at 40 C.
621	....	8	14.52	.....	4.42	.....	Left hand in water at 10 C.
2,537	2,848	18	22.34	25.15	4.69	5.31	Tumor of right forearm.
506	556	18	5.15	5.70	1.08	1.19	Hands Hodgkin's disease
3,030	3,139	22	20.79	32.89	2.34*	2.50†	Feet with edema of
1,159	1,282	17	13.57	14.90	2.82	3.22	Hands legs and feet.
1,183	974	10	22.76	17.20	1.89	1.56	Feet Trophic disturbance
486	470	9	51.62	47.03	10.62	10.00	Hands in left leg.
385	375	7	27.14	27.80	7.05	7.41	Right arm shorter than left.
4,041	1,580	9	69.19	24.61	11.93†	4.92	Infected right hand.
2,600	....	7	64.67	.....	11.15†	.....	Left hand in water at 9.2 C.
1,845	....	5	70.33	.....	12.12†	.....	Left hand in water at 4.3 C.
1,661	684	9	31.40	12.60	6.88‡	3.07	Gout; right hand.
242	....	2	21.27	.....	4.66‡	.....	Left hand in water at 4.3 C.
1,245	....	5	45.06	.....	9.88‡	.....	Left hand still in water at 4.3 C.
312	....	2	28.98	.....	6.35‡	....	Left hand in water at 8 C.
554	....	6	17.50	.....	3.84‡	.....	Left hand still in water at 8 C.
3,096	1,899	11	57.06	33.36	10.76§	8.13	Right hand worse than before.
1,443	....	9	36.43	.....	6.87§	....	Left hand in water at 8.3 C.
1,988	....	9	55.15	.....	10.40§	.....	Left hand in water at 42.8 C.
700	2,180	12	8.20	25.87	1.7	5.20	Sprain of left hand.
710	710	7	15.52	15.54	3.18	3.40	Inflamed right elbow.
1,690	1,903	16	17.08	18.16	4.81	4.78¶	Edema of left hand.
2,118	2,244	13	29.54	31.76	6.25	7.09	After bandaging left hand.
3,380	2,950	9	62.48	54.60	12.86	11.61	After bandaging left arm.
3,066	2,499	9	66.70	51.53	13.31	10.96	Second period.
2,187	1,972	5	84.51	76.09	17.98	16.65	
1,701	1,695	5	73.11	72.31	15.55	15.82	After putting band on right arm.
1.631	1,663	6	63.73	63.67	13.56	13.93	Band still on right arm.
2,430	2,348	9	71.43	67.82	15.20	14.84	After removing hand.
1,262	1,016	8	25.62	20.28	9.08	8.81	Left hand smaller than right.
.....	852	8	.....	17.59	.....	7.51	Right hand in water at 8.3 C.
.....	787	8	.....	16.71	.....	7.26	Right hand in water at 4.3 C.
979	711	10	15.5	11.22	5.96	6.6	Congenital defect of left hand.
.....	1,034	13	.....	12.90	.....	7.59	Right hand in water at 42.8 C.
.....	388	8	.....	8.04	.....	4.73	Right hand in water at 13 C.
2,188	1,547	10	40.65	27.54	7.20	5.34	Left hand partially amputated.
162	540	5	5.69	19.16	1.50	5.32	After ligation of innominate.
278	967	11	4.44	15.23	1.12	5.32	Last five minutes in calorimeter.
373	1,179	11	6.76	21.85	1.83	4.23	Whole period in calorimeters.
3,708	4,236	23	35.05	41.17	8.26	6.38	
85	.....	2	10.24	.....	2.41	10.69	Left hand in water at 10.5 C.
532	....	5	26.27	.....	6.19	....	Left hand still in water at 10.5 C.

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for the left.

13.27

The flow in the right hand came out 8.26 grams per 100 c.c. per minute and in the left 10.69 grams, for a period of twenty-three minutes, with average room temperature 26.2 C., almost the same temperature as at the first examination. The flow in both hands was considerably increased. It must be remembered that not only was the patient much stronger than when examined before, but that instead of being brought from her bed for the observations, she had come several miles on the street car. Her pulse was strong and at the rate of 104 per minute. Both hands were larger than before (right 424 c.c., left 385 c.c.).

The fact that the collateral circulation was much freer than before is particularly shown in the increase of the ratio of the flow in the two hands from 1:3.5 to 1:1.3. It is fully as well brought out by the result of the examination of the vasomotor reflexes. Immersion of the left hand in cold water caused a great diminution in the flow in the right — for the first two minutes to 2.41 grams per 100 c.c. per minute. For the next five minutes the flow was only 6.19 grams per 100 c.c. per minute, and then began to increase abruptly. Reflex vasoconstriction, therefore, was capable of markedly altering the flow in the right hand. The relative resistance of the smaller vessels of the anterior limb and of the collateral paths leading to it has accordingly changed, and the resistance in the latter does not now make up such a large proportion of the total resistance as before.

In early brachial neuritis it is usual to see a greater flow in the hand of the affected side than in that of the sound side (partial loss of vasoconstrictor tone) and the crossed vasomotor reflex to cold is intense. It is possible that in this patient part of the increase of the flow in the right hand since the last examination is due to this factor, and the good reflex vasoconstriction agrees with this.

SUMMARY

The observations in this paper were partly undertaken as tests of the technic of the method and do not lend themselves to a complete summary.

1. In a man with healing burns on the hands the apparently great vascularity of the new tissue did not correspond to an abnormally great flow. Certain phenomena interpreted as due to a peculiar vasomotor instability of the new vessels were observed in testing the vasomotor reflexes.

2. A relatively good flow in the feet was seen in a man with great and persistent edema of both legs in whom a diagnosis of Hodgkin's disease was made. This was interpreted as indicating obstruction rather on the lymph path than on the venous path.

3. Three cases of unilateral inflammation in the hand, one bacterial and two non-bacterial (gout and a sprain) were compared. The flow in

the infected hand was increased, while in the normal hand it was diminished. In the case of gout, while the flow in the inflamed hand was greater than in the normal hand the difference was much less than in the case of infection. The contralateral vasoconstrictor reflexes from the normal to the inflamed hand were very slight in the case of the infected hand; of normal intensity in the case of gout. It is suggested that this indicates the existence of a relative vasoconstrictor block in bacterial inflammation in the interests of a permanently large flow of blood to combat the infection.

4. Temporary anemia of the hand (produced by bandaging) was followed by a moderate increase in the flow in a normal man.

5. In cases of congenital differences or differences originating in early life between the two hands, the blood-flow in the defective hand corresponded to its functional condition, being of normal magnitude when the power of the hand was good.

6. In a case in which some of the fingers of one hand had been lost by amputation, the flow per unit of volume was distinctly less in the defective than in the intact hand. This is mainly because the surface of the fingers is, in proportion to their bulk, so much greater than that of the rest of the hand. It is for the same reason that the flow per unit of volume is much greater in the distal half of the normal hand than in the hand as a whole.

7. In a case in which the innominate and the right common carotid arteries had been ligated one month previously, the flow in the right hand was two-sevenths of that in the left, although no pulse could be felt in the radial. Sixteen weeks later the ratio had risen to 1:1.3, the flow in the left hand being normal in amount.

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Studies on the Circulation in Man

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STUDIES ON THE CIRCULATION IN MAN

X. THE BLOOD-FLOW IN THE HANDS IN DISEASES OF THE HEART *

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CLEVELAND, O.

GENERAL REMARKS

It has been mentioned in the introduction to the last paper[1] that when proper precautions are taken there is a very fair degree of constancy in the results obtained in successive observations on different days on one and the same patient, provided gross changes in his clinical condition are excluded. Accordingly, a marked change in the flow not accounted for by changes in the external conditions, especially in the external temperature, always suggests some decided alteration in the clinical state of the patient. On the other hand, in certain cases, information may be obtained as to the state of the patient; for example, in regard to the lability of his vasomotor mechanism or the power of adaptation of his heart, by purposely changing the external conditions or by taking advantage of changes that have spontaneously occurred, in order to determine their effect on the flow in the hands or feet.

In comparing the flows in the whole series of cases investigated with those in normal persons, one is struck by the fact that while the flow in persons suffering from well characterized pathological changes (compensated valvular lesions, for example) may be of the normal magnitude, having regard to the age of the patient, the room temperature, etc., in a much larger number of cases it is below the normal, often greatly below it. Sometimes there is good evidence that this diminution in the hand or foot flow is the expression of an increased excitation of the vasoconstrictor mechanism as a whole or at least of the portion of it which presides over the cutaneous vessels not necessarily related to any material diminution in the driving power or the output of the heart. In other cases there is good evidence that the diminished flow in the hand (or foot) is in the main the expression of diminished functional capacity on the part of the heart, associated either with engorgement of the veins

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* From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University.

[1] Paper IX of this series.

and the right side of the heart or with diminution in the filling of the arteries without increased venous pressure. In still other cases evidence may be obtained of a diminished flow in one or both hands or feet, which is solely or mainly a local condition. A local increase in the flow may accompany such conditions as inflammation or vasomotor paralysis.

The question whether the flow in the hands or feet gives any indication of the functional capacity of the heart would be best discussed on the basis of an experimental comparison of the heart output, as determined gasometrically, with the hand flow in normal and pathological cases. Even in the absence of such a comparison, however, it would appear, that where the hand (or foot) flow is not less than normal it is only in exceptional conditions (local vasomotor paralysis of hands and feet?) that any gross error will be made in assuming that the heart is discharging an amount of blood not inferior to the normal. When, however, the flow in the extremities is permanently and decidedly less than normal, several points have to be considered. In many of these cases in which the normal ratio of the hand flow to the foot flow is preserved[2] in spite of the diminution in the flow and in which no anemia is present, there is often good evidence that the lessened driving power of the heart is primarily responsible for the diminished flow. On the other hand, in the anemias[3] the diminution of the flow in the hand and in the skin generally seems to be a compensating mechanism which permits an even increased quantity of blood to be sent by the heart through the lungs.

A marked disturbance of the normal ratio between the hand and foot flow, of course, gives no information as to the functional capacity of the heart, but indicates in the absence of local anatomical changes which might account for the difference (arteritis, paresis, etc.), a change in vasomotor excitability. Usually, this is manifested in a vasoconstriction of the feet, and a foot flow smaller than the normal in comparison to the hand flow. Since the feet are normally but little exposed in comparison with the hands, local vasoconstriction connected with the technic of the measurements is more likely to occur in the feet than in the hands. In various pathological conditions, for instance, fever,[4] where the vasoconstrictor mechanism of the skin is abnormally excitable the tendency of vasoconstriction in the feet on exposure is intensified. For this reason, as well as on account of the inferior flow per unit of volume in the feet, measurements of the hand flow are always to be preferred to measurements of the foot flow when the object is to obtain general information concerning the circulation and not to study local circulatory conditions. A disturbance of the normal ratio between the hand and foot flow, due not to vasomotor, but to anatomical causes (arteritis obliterans, for example), would be revealed by the fact that the ratio remains permanently abnormal even when the external conditions, the room temperature especially, are changed so as to abolish vasomotor differences of the lower and the upper extremities, or when this is done by the administration of vasodilator drugs.

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[2] See Paper VII of this series, Jour. Exper. Med., 1913, xviii, No. 1.

[3] Paper VI of this series, Jour. Exper. Med., 1913, xviii, No. 2.

[4] See Paper VIII of this series, Jour. of Exper. Med., 1913, xviii, No. 4.

A few words are necessary in regard to the classification of the cases dealt with in this paper. Some overlapping between the groups is unavoidable and the attempt has been made to assign each case presenting a complication of lesions to the group in which the factor seemingly predominant in the clinical picture would place it. For example, in the group of myocardial affections, cases are necessarily included in which there were definite and demonstrable valvular lesions. Thus certain cases with mitral stenosis (and insufficiency) are placed in the myocardial group because there is evidence that auricular fibrillation was also present, and that probably this condition with the consequent marked disturbance of the action of the ventricle was at the time of the investigation a more important factor in the clinical situation than the valvular lesion, or at least a factor which differentiated the case from one with the valvular lesion alone, and gave to it an added gravity. Among the few cases classed as arteriosclerosis, a group which might, of course, have been greatly swollen at the expense of the other groups had attention been paid solely to this condition, is one[5] which might also have gone with the valvular lesions. It is included with the cases of arteriosclerosis simply because that condition was extremely marked in the accessible arteries.

I. CONDITIONS IN WHICH SIGNS OF INVOLVEMENT OF THE MYOCARDIUM PREDOMINATED

There is probably no pathological condition of the heart in which such small hand flows are encountered as in this group. While the myocardium is acting well, grave valvular defects may, as is well known, be overcome, and the output remain for long periods quite at the normal level. The results of the blood-flow measurements in many cases of valvular lesions with good compensation are perfectly normal. With a heart whose myocardium is seriously crippled, even when the valves are anatomically and probably functionally intact, the hand flow may sink to astonishingly small figures. Nor is this difficult to understand. A pump with somewhat leaky valves may still deliver a good stream when the strokes are strong and regular. No matter how tight the valves are the output will be small if the stroke is feeble, uncertain and irregular.

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[5] Fred. S., Paper XI of this series.

Thus in Stephen F., a man 31 years old, the flow in the hands was only 0.2 gram per 100 c.c. of hand per minute with a room temperature of 23.5 C. increased to 0.5 gram in the right hand during immersion of the left in warm water, or not more than one-twentieth of the normal flow. The protocol of this case has already been published.[6]

The man, a contractor in a small way for brick and carpenter work, was examined in the dispensary and was admitted the same day to Lakeside Hospital where he died a few days later. He stated that between three and four years previous to admission he became ill after a heavy lift and had never been well since. All the signs of cardiac failure were present. To the left the cardiac dulness extended almost to the anterior axillary line. There was marked arhythmia with numerous premature contractions. For some time past he had been aware of the irregular action of his heart and stated that it sometimes stopped for a beat. The pulse-rate was only 60 (counted at the apex beat with the stethoscope). The neck veins were much engorged in the supine position. There was edema of the feet and ankles. The hands and feet were habitually cold although the weather was mild. The whole surface was pale and cool. There was no indication of valvular lesions. No murmurs were detected during the time the patient lived. The lungs were clear. The clinical diagnosis was myocarditis without valvular lesion. The immediate cause of death was pontine hemorrhage. At autopsy the findings were fibrous myocarditis with relative insufficiency but no valvular lesion, pericarditis, perihepatitis and atrophic cirrhosis of the liver, and acute pulmonary edema.

In Mrs. A., a woman aged 72, who came to the dispensary complaining of palpitation of the heart and irregular pulse, the blood-flow in the left hand came out 0.78 gram per 100 c.c. per minute, and in the right 0.45 gram, with room temperature 22.5 C. It must be taken into account that the hands in this case, being the typical hands of old age, consisted largely of bone, which has a small blood-flow.

The irregularity of the heart has been noticed for the past six years. The heart sounds were clear and no murmurs could be detected, but there was marked arhythmia. The pulse rate was 92 in sitting position. There was no edema, no cough. There was a history of rheumatism at 50 years of age, and again the winter before admission. The hands were very thin and rather cool, although she wore gloves and said they were as warm as usual. A diagnosis of senile heart with chronic myocarditis, arhythmia and arteriosclerosis was made She continued to come periodically to the dispensary for over four months, still complaining of palpitation although the pulse became more regular.

The difference in the flow in the two hands (it must of course be noted that the accuracy of the measurements is less with these small flows than with normal flows) suggests that the smallness of the flow may be partly due to local vasoconstriction, which is often temporarily unequal for the two hands, and not altogether to the small output of the heart. The question may indeed be raised whether as in the anemias[7] a peripheral constriction may not occur in these cases in the interest of an increased flow through the lungs (and through the brain and other vital organs). In some ways the question is merely an academic one, since it is well known that in marked anemia the heart muscle may be impaired. It is clear that the percentage content and the total absolute amount of hemoglobin in the blood being normal, there may still be oxygen deficiency if the weakened heart is unable to propel the normal amount of blood from the left ventricle through the systemic vessels to the right side of the heart. On the supposition that the right ventricle could deal with a larger quantity of blood than is actually brought to it, a diminution in the average circulation time of the blood through the systemic path brought about by vasoconstriction confined to or predominating in the periphery might increase the minute volume of the heart. In this case the small hand flow, where the myocardium is seriously damaged, would be due to two things: First, diminished driving power of the heart; and second, constriction of the vessels of the peripheral parts in excess of that which would correspond to the diminished filling of the vessels due to the deficient action of the heart alone. Although the output in such cases as Stephen F. is diminished, it is not conceivable that it is diminished in the same proportion as the hand flow.

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[6] Cleveland Med. Jour., 1911, x, 385.

[7] Jour. Exper. Med., 1913, xviii, No. 2.

Jacob W., a house carpenter aged 59, height 5 feet, 1 inch, weight 173 pounds, was admitted at the dispensary April 4, 1911, suffering from myocarditis with anginal attacks. Six months previously while going to church he was suddenly seized with substernal pain, with great dyspnea. He had to sit down and could not speak. Since that time he has had a spell every morning, lasting two to five minutes and it is getting worse. If the pain is severe the left hand and forearm get dead. Since yesterday he has had palpitation. His general health was good until six months ago. He had rheumatism eighteen years ago. He used to drink beer and whisky moderately and to smoke moderately. He denies lues. Physical examination, cyanosis, some icterus; emphysema; heart generally enlarged; no murmurs. The heart sounds are weak; blood-pressure high; some sclerosis of the arteries. Urine negative.

He came periodically to the dispensary after this. April 24, 1911, his systolic blood-pressure was 190, diastolic 110. April 27, 1911, he had five attacks during the night. May 1, 1911, he had a mild attack while being examined in the dispensary. The pain was felt right beneath the sternum and radiated down the inner side of the left arm and up the neck to the chin. The pulse becomes somewhat smaller during the attack but the rate does not change. The heart is enlarged 4 cm. to the left but not to the right. He is still stout. He is being treated with potassium iodid and sodium nitrite. The blood flow in the hands was examined May 1, 1911. Mouth temperature 37.1 C. Pulse (sitting) 100, and rather small. Hands in bath at 2:44 p. m., in calorimeters at 2:55.* At 3:10 p. m. left hand put into water at 42.9 C. (Table 1.)

Cooling of calorimeters, R., 0.11 degrees in fourteen and one-half minutes; Left 0.14 degrees in twenty-one and one-half minutes. Volume of right hand, 508 c.c., of left hand 486 c.c. The hands were fat.

The flow in the right hand works out at 2.46 grams per 100 c.c. per minute, and in the left hand at 1.96 grams. When the left hand was immersed in warm water the flow in the right rose to 3.86 grams, a fair reflex vasodilatation. Subsequent immersion of the left hand in cold water caused little change in the flow in the right.

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* Three thousand and fifteen c.c. of water were put into each calorimeter. In the protocols, unless otherwise mentioned, this was the quantity always used for the hand calorimeters.

TABLE 1.—CALORIMETRIC MEASUREMENTS IN CASE OF JACOB W.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
2:54	29.83	29.91	24.1	3:14	30.12	
2:56	29.81	29.86	.....	3:15	30.14	
2:57	29.82	29.86	.....	3:16	30.18	
2:58	29.84	29.87	.....	3:17	30.20	Room 25.0 C.
2:59	29.87	29.88	24.9	3:18	30.23	
3:00	29.87	29.89	.....	3:19	30.26	
3:01	29.88	29.91	.....	3:20	30.29	At 3:20 left hand put in water at 11.5 C.
3:02	29.89	29.92	.....	3:21	30.32	Room 25.1 C.
3:03	29.89	29.92	.....	3:22	30.34	
3:04	29.91	29.93	25.0	3:23	30.36	
3:05	29.92	29.94	.....	3:24	30.39	
3:06	29.93	29.94	.....	3:25	30.41	
3:07	29.95	29.95	.....	3:26	30.44	
3:08	29.98	29.97	.....	3:27	30.47	Left hand dried and wrapped.
3:09	29.99	29.98	.....	3:28	30.49	Room 25.1 C.
3:10	30.02	30.00	.....	3:29	30.51	
3:11	30.03	.....	.....	3:30	30.54	Hand out of calorimeter at 3:30.
3:12	30.05	.....	.....	3:31½	.....	Temp. of L. is now 29.86 C.
3:13	30.08	.....	25.2	3:44½	30.43	Temp. of L. is now 29.76 C.

In James M., a man 60 years old, with a very irregular pulse, enlarged heart and a history of edema of the feet and legs, the flow was 1.99 grams per 100 c.c. per minute in the right hand, and 1.35 grams in the left (for the last ten minutes in the calorimeters). Anemia was probably not an important factor in the small blood-flow, since the hemoglobin content of the blood was 80 per cent. three days before the examination. The calculated flows for the last twenty minutes in the calorimeters are 1.56 grams per 100 c.c. per minute and 1.06 grams for the right and left hands respectively, the ratio between the flows being precisely the same as for the last ten minutes (1.47:1).

James M., a laborer aged 60, was admitted to the City Hospital June 16, 1912. Three weeks before when in another hospital his feet and legs swelled and pitted on pressure. On admission to the City Hospital petechiae were present on both legs but there was no edema. The right side of the chest lags in inspiration and shows diminished resonance beginning at the sixth interspace in the axillary line, and also posteriorly. Fifteen months ago he had dyspneic attacks and the right pleural cavity was tapped. June 21, 1912, the right chest was aspirated but no fluid was obtained. The left border of heart dulness is outside the nipple line, the right border at the right margin of the sternum. The first sound is roughened. Pulse irregular, arhythmic, fair volume, sclerosis marked. The rectal temperature since his admission has varied from 100.4 to 98.2 F.

Examination of the blood-flow in the hands was made June 27, 1912, on which day he was discharged. Hands in bath at 1:34½ p. m.; in calorimeters at 1:43¾ p. m., and out of calorimeters at 2:15.

TABLE 2.—CALORIMETRIC MEASUREMENTS IN CASE OF JAMES M.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
1.43	31.02	31.12	.....	2.01	30.93	30.97	....
1.45	30.99	31.09	.....	2.02	30.93	30.965	....
1.46	30.98	31.08	22.9	2.03	30.93	30.955	23.0
1.47	30.98	31.07	.....	2.04	30.925	30.95	....
1.48	30.975	31.06	22.9	2.05	30.925	30.945	....
1.49	30.97	31.05	.....	2.06	30.93	30.94	23.1
1.50	30.965	31.04	23.0	2.07	30.925	30.935	....
1.51	30.96	31.03	.....	2.08	30.925	30.93	....
1.52	30.96	31.03	.....	2.09	30.93	30.93	23.1
1.53	30.955	31.025	23.1	2.10	30.925	30.93	....
1.54	30.95	31.02	.....	2.11	30.93	30.925	....
1.55	30.95	31.015	.....	2.12	30.925	30.925	....
1.56	30.94	31.005	23.1	2.13	30.93	30.925	23.0
1.57	30.94	31.00	.....	2.14	30.93	30.92	....
1.58	30.94	30.995	.....	2.15	30.925	30.915	....
1.59	30.935	30.99	.....	2.27	30.795	30.78	....
2.00	30.935	30.98	23.2				

Cooling of calorimeters in twelve minutes, R., 0.13 degrees; L., 0.135 degrees. Volume of right hand 368 c.c., of left hand 356 c.c. He is right handed,* wrists very thin, hands skinny. Pulse 87 (sitting). Very irregular. Rectal temperature 37.65 C. Water equivalent of calorimeters with contents, R., 3,389; L., 3,380. Blood-pressure, systolic 149 (palpation), 152 (stethoscope), 72 (sound gone). Another observation, systolic 144 (palpation).

A case diagnosed as auricular fibrillation (in N. P) is included under this heading, although there was a valvular lesion (mitral stenosis) present as well. The case did not come under my observation until the patient had improved considerably under treatment (digitalis), yet even then the flow in the hands was quite small for her age (1.97 grams per 100 c.c. per minute for the right hand, and 1.59 grams for the left for the last eleven minutes in the calorimeters). The small flow agreed with the persistent coldness of the hands and feet. It was not associated with anemia.

N. P., aged 27, was admitted for her present illness to the City Hospital March 12, 1913. (She was first admitted to the hospital April 4, 1910, suffering from rheumatism.) Heart: Apex beat visible in fifth interspace, one finger's breadth outside the nipple line. A presystolic thrill can be felt here. Left border two finger's breadth outside the nipple line; right border at the midsternal line, upper border at third rib. A rough presystolic murmur is heard over a small area at the apex. All over the precordia and transmitted to the axilla and back is heard a soft systolic murmur. The pulse shows marked arhythmia. Considerable edema. The urine, March 13, 1913, contained neither albumin nor casts. On May 12, 1913, there was some albumin but no casts. Under treatment (including digitalis) the pulse rate diminished. The arhythmia became less marked although it did not disappear, and the edema cleared up. Her appetite continues poor, but she sleeps well and is not troubled with dyspnea in any position. Her hands and feet are always cold. She says she is only really warm when surrounded by hot water bottles. Polygraph tracings from the jugular and radial taken on May 16, 1913, showed the ventricular form of venous pulse, "*a*" waves being absent from the jugular tracing. The rate of the heart in the semi-reclining position was 80 as counted at the apex with the stethoscope, and precisely the same at the wrist. The variation in the duration of successive beats is great. Twelve successive beats were measured in each of two portions of the tracing. In the first series the durations were 1.1, 0.8, 0.9, 0.8, 0.7, 0.65, 0.65, 0.5, 0.6, 0.9, 0.75, 0.9 second, the average being 0.77 second corresponding to 78 beats per minute. In the second series the durations were 0.85, 0.65, 0.75, 0.7, 0.7, 0.55, 0.75, 0.85, 0.9, 0.85, 0.95, 0.85 second, the average being 0.78 second corresponding to 77 beats per minute.

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* It can always be assumed that a patient was righthanded unless the contrary is stated in the protocols.

The blood-flow was examined May 12, 1913. Hands in bath at 2:43 p. m.; in calorimeters at 2:54½, and out of calorimeters at 3:16. Mouth temperature 36.3 C. (the thermometer was in five minutes and special care was taken).

TABLE 3.—CALORIMETRIC MEASUREMENTS IN CASE OF N. P.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.54	31.56	31.41	.....	3.06	31.455	31.28	23.9
2.55	31.53	31.37	.....	3.07	31.45	31.27	....
2.56	31.51	31.36	24.2	3.08	31.45	31.27	....
2.57	31.50	31.355	.....	3.09	31.44	31.26	....
2.58	31.50	31.35	24.1	3.10	31.43	31.255	23.8
2.59	31.49	31.34	.....	3.11	31.43	31.25	....
3.00	31.49	31.33	.....	3.12	31.42	31.24	....
3.01	31.48	31.31	.....	3.13	31.42	31.235	....
3.02	31.46	31.30	.....	3.14	31.41	31.23	....
3.03	31.46	31.29	23.6	3.15	31.41	31.225	....
3.04	31.46	31.285	.....	3.16	31.405	31.215	....
3.05	31.455	31.28	23.9	3.35	31.19	30.995	....

Cooling of calorimeters in 19 minutes, R., 0.215 degrees; L., 0.22 degrees. Volume of right hand in calorimeter 298 c.c., of left hand 276 c.c. Pulse (sitting) 75 in one count, 66 in another, irregular and weak. It is not easy to count the pulse at the wrist because of the variability in the beat. Systolic blood-pressure in right arm 95. Difficult to determine the blood-pressure with the stethoscope.

A man 44 years old (Jacob S.), with mitral stenosis and insufficiency, an irregular heart, and weak and irregular pulse, from a study of whose case a diagnosis of auricular fibrillation was made, had a flow of only 1.97 grams per 100 c.c. per minute in the right hand, and 0.96 gram in the left, with room temperature 22.2 C. The disproportion in the flow in the two hands is associated with old hemiplegia of the left side. Immersion of the right hand in warm water caused a great percentile increase in the flow in the left hand (to 1.54 grams per 100 c.c. per minute for the first five minutes and 3.86 grams for the next four minutes), although the maximum was still absolutely a small flow. The fair crossed vasomotor reflex from the normal to the formerly paralyzed hand, which had largely recovered, contrasts with the absence of reflex in a case of old hemiplegia where there had been no recovery of the hand.[8]

Jacob S., a tailor aged 44, height 5 feet, 3½ inches, weight 140 pounds, first presented himself at the dispensary Oct. 27, 1910. Three years before he had rheumatism and had "heart trouble" at that time and also pneumonia. Eleven years ago when sitting in a chair he had a left-sided paralysis which came on him suddenly. He lost consciousness. He also had aphasia. He could understand what was said but could not speak. He recovered his speech in two months. The arm and leg recovered slowly. There was no disturbance of sensation at the time of the stroke, but two months later he had loss of sensation so that a pin could be stuck into his arm or leg without his knowing it. He burnt his left elbow severely without feeling it by leaning on a stove. The lines on the left side of the face are not so deep as on the right. He drags the left foot somewhat. The tongue is protruded in the median line. The reflexes are much increased in both upper and lower extremity. Babinski's sign can be obtained on the left side. Touch and pain are normally appreciated on the left side but heat cannot be distinguished over the left arm. The physical signs of chronic bronchitis and emphysema are present. Heart slightly enlarged both to right and left. Pulmonic second sound accentuated. The heart sounds are very irregular both in force and rhythm. Pulse rate 80.

Nov. 5, 1910, a marked presystolic murmur and thrill can be made out.

Dec. 10, 1910, he is very dyspneic and cannot sleep. Ears, fingers, tip of nose and lips are cyanotic. Positive venous pulse in the neck. The heart dulness extends two fingers outside the nipple line on the left side and two fingers outside the sternal margin on the right. There is a sharp first sound preceded by a faint presystolic murmur and followed by a systolic murmur. The pulse is small, irregular and of very poor volume and tension. The left radial pulse is smaller than the right. The liver is increased in size to percussion. He was received into the hospital to-day where he improved. Blood-pressure, systolic 162, diastolic 120. Blood: leukocytes, 10,500; hemoglobin, 90 per cent.

April 11, 1911, he returned to the dispensary in about the same condition as before he entered the hospital. Pulse rapid and irregular.

April 25, 1911, enlargement of the heart and arhythmia is still marked. Knee-jerk much exaggerated on the left side. When he gets out of breath he feels the left hand getting stiff. The difference in size of the two hands is not conspicuous. The great difference in the two arms is in the girth of the shoulders, the left shoulder being much smaller than the right. He cannot completely extend the left forearm on the elbow owing to contracture. Sometimes when he is grasping an object in his left hand the fingers remain closed around it involuntarily and he has to release the object with the other hand. He lost sexual power at the time of the stroke and has not regained it. He has been constipated since the stroke and has had to use cathartics constantly.

The blood-flow in the hands was measured April 25, 1911. Pulse (sitting) 104. Mouth temperature 36.25 C. Hands in bath at 2:31 p. m., in calorimeters at 2:42.

At 2:55 p. m. the right hand was put into water at 43.3 C.

Calorimeter R. was constantly stirred until 3:10 p. m. After this R. and L. were only stirred occasionally. Cooling of R. from 2:55 to 3:10½ is 0.18 degree (in fifteen one-half minutes.) Cooling of R. from 3:10½ to 3:27 (with little stirring) is 0.15 degree (in sixteen one-half minutes.) Cooling of L. from 3:10½ to 3:28 (with little stirring) is 0.16 degree (in seventeen one-half minutes.) Accordingly with little stirring L. cooled at the same rate as R. We can therefore assume that with constant stirring this would also be true and that the amount of cooling for L. during the observations is 0.18 degree in fifteen and one-half minutes. Volume of right hand 390 c.c., of left hand 378 c.c.

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[8] Heart, 1911, iii, 81.

TABLE 4.—CALORIMETRIC MEASUREMENTS IN CASE OF JACOB S.

Time	Right	Left	Temp. Room C.	Time	Left	Notes
2:41	29.73	29.72	.....	2:58	29.60	
2:43	29.68	29.65	.....	2:59	29.60	Room 22.7 C.
2:44	29.68	29.65	22.0	3:00	29.60	
2:45	29.68	29.64	.....	3:01	29.59	
2:46	29.68	29.64	.....	3:02	29.61	
2:47	29.67	29.63	.....	3:03	29.62	
2:48	29.67	29.63	.....	3:04	29.63	
2:49	29.67	29.62	.....	3:05	29.64	At 3:05 right hand dried and wrapped.
2:50	29.68	29.63	.....	3:06	29.64	
2:51	29.68	29.62	.....	3:07	29.65	
2:52	29.68	29.61	22.4	3:08	29.65	
2:53	29.69	29.61	.....	3:09	29.67	
2:54	29.69	29.60	.....	3:10	29.68	At 3:10 hand out of calorimeter.
2:55	29.70	.....	.....			
2:56	.....	29.60	22.6	3:10½	.....	Temp. of R. is now 29.52 C.
2:57	.....	29.59	.....	3:27	.....	Temp. of R. is now 29.37 C.
				3:28	29.52	

In a third case diagnosed as one of auricular fibrillation (T. F. K.), a man 57 years old, the flow was 4.45 grams per 100 c.c. per minute for the right hand, over an eighteen-minute period, and 5.23 grams for the left hand (ratio of the flows in the two hands 1:1.17). For the last nine minutes of this period, the flows were 6.21 grams and 7.06 grams, respectively, for the right and left hands (ratio of the flows in the two hands 1:1.13). These are fair flows for the man's age, indicating that the heart in spite of the irregular action of the ventricle is maintaining a fair output. This corresponds entirely with the clinical condition at the time of the blood-flow examination. The edema had completely disappeared. There was no dyspnea. The appetite was good and the patient was no longer confined to his bed. Many of the pulse beats at the wrist were of good amplitude, although others were small (Fig. 1), while in the case of N. P. all of the beats were small.

T. F. K., a bricklayer, aged 57, height 5 feet, 9½ inches, weight 140 pounds, was admitted at the City Hospital May 1, 1913. He had typhoid about thirty years ago and rheumatism sixteen or eighteen years ago. His present illness began last November. His ankles became swollen and also his legs, nearly up to the hips, and he lost strength and weight rapidly. He noticed at the same time that his pulse was irregular. He had pain in the right side of the chest. The swelling in the legs had diminished somewhat before he entered the hospital, but on admission edema and cyanosis were still to be observed. His chest was barrel-shaped with broad costal angle and poor expansion. No râles or dulness over the lungs, but there was a friction rub over the anterior surface of the right lung. The cardiac impulse was diffuse, and extended considerably beyond the nipple line on the left side. Cardiac dulness enlarged to the left. The liver was somewhat enlarged and pulsation evident in the epigastrium. The veins in the neck were distended. A systolic murmur was heard over the apex. His maximum temperature (on May 9) was 103.6 F., minimum 97.4 on the same day. The maximum temperature on May 16 was 102; May 17, 102; May 19, 101.4 F. The pulse-rate on May 1 was 120; May 19, 92. The pulse-rates were usually above 90. The radial pulse is markedly irregular in amplitude and rhythm, and the irregularity is not affected when respiration is suspended. Polygraph tracings from the distended external jugular vein and the radial artery showed that the venous pulse was of the ventricular character (Fig. 1). Diagnosis, auricular fibrillation. The blood-flow in the hands was examined May 19, 1913, at which time the swelling had entirely disappeared from the lower extremities and the patient was allowed to sit up for a portion of the day. Hands in bath at 3:14 p. m.; in calorimeters at 3:26¾, and out of calorimeters at 3:47.

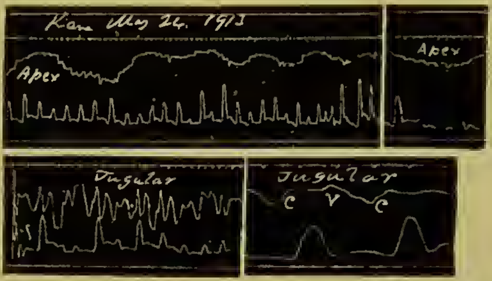

Fig. 1.—Upper part of tracing, simultaneous record of apex beat and radial pulse. The respiratory movements interfered with the apex trace except towards the end of expiration. At the right is a portion of the apex tracing which allows a sufficiently good comparison to show that some of the apex beats are only feebly represented on the radial trace. The lower portion of the figure gives simultaneous tracings from the external jugular and the radial. As in all tracings, time is marked in fifths of a second. (All tracings reduced to about one-half size of originals.)

TABLE 5.—CALORIMETRIC MEASUREMENTS IN CASE OF T. F. K.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.26	31.59	31.48	.....	3.38	31.63	31.59	24.0
3.28	31.56	31.46	23.5	3.39	31.66	31.625	....
3.29	31.565	31.47	.....	3.40	31.695	31.665	23.95
3.30	31.57	31.475	.....	3.41	31.72	31.685	....
3.31	31.57	31.48	.....	3.42	31.74	31.73	....
3.32	31.57	31.485	.....	3.43	31.78	31.76	24.0
3.33	31.58	31.50	24.2	3.44	31.79	31.77	....
3.34	31.58	31.50	.....	3.45	31.82	31.82	24.1
3.35	31.59	31.525	.....	3.46	31.84	31.86	....
3.36	31.60	31.55	.....	3.47	31.88	31.90	....
3.37	31.62	31.56	.....	4.16	31.52	31.555	....

Cooling of calorimeters in 29 minutes, R., 0.26 degrees; L., 0.245 degrees. Volume of right hand in calorimeter 444 c.c., of left hand 458 c.c. He is left handed. Water equivalent of calorimeters with contents, R., 3,450; L., 3,461.

Rectal temperature 37.35 degrees. Blood-pressure in left brachial, maximum systolic (when the larger pulsations begin to be heard) 111, 58 (sound gone). Another observation, maximum systolic 114, 58 (sound gone).

In two cases in which acute symptoms diagnosed as due to myocarditis had been present, but which had markedly improved under treatment so that the patients were able to come without trouble to the dispensary, a fair hand flow was found. Both were men 59 years old. In one of these patients (J. S. W.) who had been in the hospital two years before and had been near death, the flow was 6.82 grams per 100 c.c. per minute in the right hand and 6.58 grams in the left, with room temperature at 21.9 C. Simultaneous tracings from the jugular bulb, the radial artery and the apex showed that the *"c"* wave was notably large; the *a* wave was also well marked. All the ventricular beats were recognizable on the radial trace.

J. S. W., a fireman, colored, height 5 feet, 10 inches, weight 160 pounds, born in 1851, was first admitted to the dispensary Feb. 21, 1905, complaining of pain in chest and cough. The heart sounds were faint but clear. No murmurs. Heart dulness enlarged to the left well beyond the mammary line. The pulse was irregular. A diagnosis of myocarditis was made. April 13, 1908, he was again admitted to the dispensary. Heart enlarged to the left two fingers breadth beyond the mammary line. Pulse rapid and irregular. Some albumin in the urine. Nov. 4, 1908, he was admitted to Lakeside Hospital and again on Feb. 20, 1909. He had attacks of syncope with fluttering in the chest and came near death. The pulse-rate was 120, systolic blood-pressure 160. Pulse regular and all the beats reached the wrist. Under treatment the pulse rate diminished and as it slowed the arhythmia returned (premature contractions). March 19, 1909, the rate was 68, systolic blood-pressure 160. Tracings from the bulbus venosus showed well marked *a*, *c* and *v* waves of which the *c* wave was very large. Presystolic, systolic and diastolic pulsations were visible over the jugular bulb. He was discharged from the hospital May 5, 1909, improved. Oct. 5, 1909, he reported at the dispensary that he had gained 20 pounds since leaving the hospital. Oct. 4, 1910, he was feeling better, but had occasional smothering sensations. There was now no arhythmia and no albumin in the urine.

TABLE 6.—CALORIMETRIC MEASUREMENTS IN CASE OF J. S. W.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.10	29.40	29.29	.....	3.22	29.96	29.86	....
3.14	29.47	29.38	.....	3.23	30.00	29.91	....
3.15	29.53	29.43	.....	3.24	30.08	29.97	....
3.16	29.59	29.50	.....	3.26	30.20	30.10	....
3.17	29.66	29.55	.....	3.27	30.23	30.12	....
3.18	29.73	29.61	.....	3.34	30.16	30.06	....
3.19	29.78	29.67	.....	3.39	30.09	30.00	....
3.20	29.83	29.71	.....	3.51	29.96	29.88	....
3.21	29.89	29.80	.....				

The flow in the hands was measured Jan. 10, 1911. He feels much improved. Systolic pressure still very high; when last taken 210. Hands in bath at 3:00 p. m.; in calorimeters at 3:11½, and out of calorimeters at 3:27; 3,050 c.c. of water in each calorimeter. Room temperature 21.7 C. (Table 6.)

Volume of right hand 570 c.c., of left hand 570 c.c. His hands are very large. Pulse 60 (sitting). Mouth temperature 36.5 C. Rectal temperature 37.6 C. Room temperature at end of observations 22.2 C.

Since this time he has continued to report at the dispensary and has been more than once in the hospital with the signs of cardiac breakdown. On Dec. 7, 1912, "the left border of the cardiac dulness is at the anterior axillary line, and the right one finger's breadth beyond the right sternal border, heart thumping and somewhat irregular. Feb. 11, 1913, spitting blood and short of breath. Right border of cardiac dulness two fingers breadth to right of sternal margin. Sounds distant and irregular. No murmurs. Râles throughout both lungs." In June, 1913, eight years from the beginning of his illness, he was still coming to the dispensary and had periods of temporary improvement.

The other patient (Peter B.) was twice examined. At the first examination he had a flow of 6.44 grams per 100 c.c. of hand per minute in the right hand and 5.99 grams in the left, with room temperature 24.5 C. This is by no means a large flow for the temperature, and while fair reflex vasodilatation was obtained by the application of warmth to the contralateral hand, cold did not cause vasoconstriction sufficient to reduce the flow to the initial amount. This agrees well with the fact that arteriosclerosis was distinct, for reflex vasoconstriction is not well obtained in this condition. Almost a month later his hand flow was again measured. He had meanwhile much improved. The flow was 9.95 grams per 100 c.c. per minute for the right and 7.46 grams for the left hand. However, the room temperature was relatively high (26.6 C.), and this probably accounted for a portion of the increase in the flow. The vasodilatation consequent on the high external temperature was considerable and permitted a small reflex vasoconstriction when the contralateral hand was immersed in cold water.

Peter B., a janitor, aged 59, height 5 feet, 2 inches, weight 126 pounds, was under observation at the dispensary with symptoms diagnosed as due to myocarditis. For many years he did heavy work in a gas works. Though his work is now light he has had to give it up for the present. He suffered greatly from rheumatism till about fifteen years ago, since which time he has not been troubled. His joints would swell and he could not walk. He is married and has seven children, all in good health. His present illness dates from somewhat less than two years ago, when he suddenly became unconscious while mowing the lawn. He remained unconscious for five minutes. Three months later he had another attack. He came to the dispensary a number of times, and the records state that he had a slow pulse (60 a minute). The intervals between attacks became gradually shorter, and they occurred about once in six weeks. He falls down and "goes stiff" (extensor spasm) and now he sometimes has two attacks in a week. He seems particularly liable to become unconscious in bed. When he arises after bending down he is blind for about two minutes. Pupil reactions to light and accommodation are normal. He has long suffered from chronic bronchitis. Since the present trouble began his feet are always cold. Previously they used to be very hot and perspired greatly. He does not feel that his hands are cold. Physical examination negative for lungs. Heart dulness two finger's breadth to left of nipple. Sounds clear, distant, the first a little shortened. No accentuation of aortic or pulmonary. Arteries somewhat thickened. Pulse slow, fair volume, well sustained, easily compressible; rate 62. Marked slowing when the vagi are compressed in the neck. There is a venous pulse in the neck.

The flow in the hands was first examined April 21, 1911. Pulse (sitting) 80. Mouth temperature 36.45 C. Room temperature 24.8 C. Hands in bath at 2:31½ p. m., in calorimeters at 2:42. At 2:53 left hand put into water at 42.9 C.

TABLE 7.—CALORIMETRIC MEASUREMENTS IN CASE OF PETER B.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
2:40½	30.04	30.03	.....	3:00	30.57	
2:43	30.01	30.02	.....	3:01	30.60	
2:44	30.03	30.03	24.7	3:02	30.63	
2:45	30.06	30.06	.....	3:03	30.69	At 3:03 put left hand in water at 8 C.
2:46	30.09	30.09	.....	3:04	30.71	Room 24.3 C.
2:47	30.11	30.10	.....	3:05	30.77	
2:48	30.14	30.12	.....	3:06	30.79	
2:49	30.17	30.14	.....	3:07	30.81	
2:50	30.20	30.18	.....	3:08	30.83	
2:51	30.24	30.21	24.3	3:09	30.87	
2:52	30.28	30.23	.....	3:10	30.89	
2:53	30.30	30.25	.....	3:11	30.91	At 3:11 dried left hand and exposed it for inspection. Then wrapped it in warm cloth.
2:54	30.32	.....	.....	3:12	30.93	
2:55	30.36	.....	24.4	3:13	30.97	
2:56	30.40	.....	.....	3:14	31.00	Room 24.2 C.
2:57	30.44	.....	.....	3:15	31.04	Hand out of calorimeter at 3:15.
2:58	30.49	.....	24.2	3:30	30.89	At 3:30 temp. L. 29.95 C.
2:59	30.52	.....	.....			

Cooling of calorimeters, R., 0.15 degree in fifteen minutes; L., 0.30 degree in thirty-seven minutes. Volume of right hand 360 c.c., of left 320 c.c. Water equivalent of calorimeters with contents, R., 3,383; L., 3,351.

Second examination May 17, 1911. He is feeling much better than when last examined. He was being treated with potassium iodid and nitroglycerin. Although he has had slight attacks of dizziness and "feeling stupid," he has not fallen or "gone stiff." There is no arhythmia now, nor can any murmurs be detected. Pressure on the vagus in the neck readily inhibits the heart causing the pulse at the wrist to disappear for a beat or two. He feels dizzy during the compression, and he can be made unconscious at any time by pressing on the vagus.

Hands in bath at 2:33 p. m., in calorimeters at 2:43½; mouth temperature 36.5 C.; pulse (sitting) 84. At 2:55 p. m. left hand put into water at 8 C.

Cooling of calorimeters, R., 0.07 degree in ten minutes; L., 0.17 degree in twenty-nine minutes. Volume of right hand in calorimeter 410 c.c., of left hand 394 c.c. The marks were put higher up than usual as his hands were short. The lower mark was about the middle instead of the lower border of the styloid process of the ulna. He seemed gradually to improve and reported at his last visit to the dispensary, June 7, 1911, that he was better. Pulse 84. (See Table 8.)

II. VALVULAR LESIONS

The flow in these cases may be normal or much less than normal, depending on the degree of compensation. Since anemia may be associated with a valvular lesion, it may be a factor in diminishing the hand flow in the way already discussed in a previous paper.[3] Since, further, the degree of involvement of the myocardium will differ in different cases with one and the same valvular lesion, it is not to be expected that a relatively large flow should always be associated with one particular type of valvular defect and a small flow with another. Nevertheless, so far as can be judged from the series of cases examined, certain of the valve lesions are more apt to be associated with the normal flow than others or even with a flow somewhat above the normal. Mitral insufficiency, for instance, it would seem, is less likely to be associated with a diminished hand flow than aortic insufficiency. In the only case in which a diagnosis of pure aortic stenosis seemed justified, the hand flow was normal, and this agreed with the clinical condition of the patient, who indeed did not enter the hospital for his heart lesion, but for a surgical cause. To emphasize the fact, however, that the mere naming of the valvular lesion is no indication of the amount of the hand flow, we shall begin the description of this group of cases with one of mitral incompetence in which the flow was very markedly diminished.

TABLE 8.—CALORIMETRIC MEASUREMENTS IN CASE OF PETER B.
SECOND TEST

Time	Right	Left	Room Temp. C.	Time	Right	Notes
2:43	30.29	30.18	.....	3:00	31.125	
2:45	30.35	30.22	26.4	3:01	31.16	
2:46	30.42	30.27	.....	3:02	31.195	
2:47	30.51	30.32	.....	3:03	31.23	
2:48	30.57	30.38	26.5	3:04	31.29	
2:49	30.63	30.425	.....	3:05	31.325	At 3:05 left hand put in water at 43 C.
2:50	30.68	30.455	.....	3:06	31.355	
2:51	30.73	30.50	.....	3:07	31.38	
2:52	30.79	30.535	.....	3:08	31.41	
2:53	30.835	30.57	.....	3:09	31.44	
2:54	30.88	30.60	.....	3:10	31.475	Room 26.7 C.
2:55	30.915	30.625	.....	3:11	31.505	
2:56	30.94	.....	.....	3:12	31.53	
2:57	30.99	.....	26.8	3:13	31.565	
2:58	31.035	.....	.....	3:14	31.59	Room 26.6 C. Hand out of calorimeter at 3:14.
2:59	31.08	.....	.....	3:24	31.52	At 3:24 temp. L. 30.455 C.

John T., contractor, aged 28, height 5 feet 6 inches, was admitted to the City Hospital March 31, 1912, with edema of the legs and hands and considerable cyanosis. A systolic murmur can be heard at the apex of the heart. The apex beat is visible and palpable with a heaving impulse in the sixth interspace in the nipple line. There is pulsation in the suprasternal notch. The cardiac dulness in the sixth left interspace is three fingers breadth outside the nipple line. The radial pulse is not easy to feel on account of the edema. It is small in volume and tension but has a regular rhythm. The urine contains albumin. He was treated with digitalis. April 9, 1912, the blood-flow in the hands was examined. Hands in bath at 2:21 p. m., in calorimeters at 2:31. He had some cough during the observations. Systolic blood-pressure 122. Pulse 70. At 2:47 p. m. left hand put into water at 42.7 C.

TABLE 9.—Calorimetric Measurements in Case of John T.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
2:30½	31.40	31.49	.....	2:48	31.385	
2:32	31.35	31.44	24.3	2:49	31.385	
2:33	31.35	31.44	.....	2:50	31.39	Room 24.3 C.
2:34	31.34	31.43	.....	2:51	31.39	
2:35	31.34	31.43	24.1	2:52	31.395	
2:36	31.335	31.425	.....	2:53	31.395	
2:37	31.335	31.425	.....	2:54	31.395	
2:38	31.34	31.43	.....	2:55	31.40	Hand out of calorimeter. Room 24.3 C.
2:39	31.345	31.435	.....	3:11	31.23	At 3:11 temp. L. 31.225 C.
2:40	31.35	31.435	.....			
2:41	31.35	31.435	24.3			
2:42	31.36	31.435	.....			
2:43	31.365	31.44	.....			
2:44	31.37	31.445	.....			
2:45	31.37	31.45	.....			
2:46	31.38	31.455	24.6			
2:47	31.38	31.455	.....			

Cooling of calorimeters, R., 0.17 degree in sixteen minutes; L., 0.23 degree in twenty-four minutes. Volume of right hand 450 c.c., of left hand 438 c.c. Water equivalent of calorimeters with contents, R., 3,455; L., 3,445. Rectal temperature 37.95 C.

April 24, 1912, he was discharged "improved."

In this case the flow was only 2.09 grams per 100 c.c. of hand per minute in the right hand, and 1.67 grams in the left, with room temperature 24.4 C., a flow very much too small for his age.

In a case of mitral stenosis, mitral and tricuspid insufficiency in a man 63 years old (James H.), the flow, measured on an exceedingly hot day with a room temperature of nearly 31 C., was 7.31 grams per 100 c.c. of hand per minute for the right hand and 6.41 grams for the left. Probably not more than one-third to one-half of the flow to be expected in a healthy young adult for that room temperature. Measurements made at such high room temperatures do not lend themselves readily to comparisons. The examination was made on this day purposely to observe the effect of maximal vasodilatation on the flow in this case, since at two previous examinations the hand flow seemed to be greatly diminished by persistent local vasoconstriction which the patient attributed to the low temperature of the wards. He said he had felt chilly all the time, but to-day he felt warm. The pulse showed arhythmia (Fig. 2), partly respiratory.

James H., a hatter, aged 63, admitted to the City Hospital May 2, 1913, suffering from chronic endocarditis with mitral stenosis and insufficiency and tricuspid insufficiency. No history of rheumatism. He complains of weakness and shortness of breath for the last three or four weeks. His feet swell at times. Ears, lips, nails and mucous membranes were markedly cyanotic on admission. There was slight edema of the legs with great varicosity of the leg veins. Marked engorgement and pulsation of the veins of the neck. Lungs revealed nothing special on physical examination. Heart enlarged. Left border of cardiac dulness at the anterior axillary line in the sixth interspace; right border 3 cm. to right of sternum. A presystolic thrill followed by impact and systolic thrill palpable over apex. Liver pulsatile and the lower edge palpable 8 cm. below the costal margin. Radial pulse markedly irregular and arhythmic with fair volume and tension, fairly well sustained. He was discharged May 17 improved. He went to work but became ill again and returned to the hospital May 23, 1913.

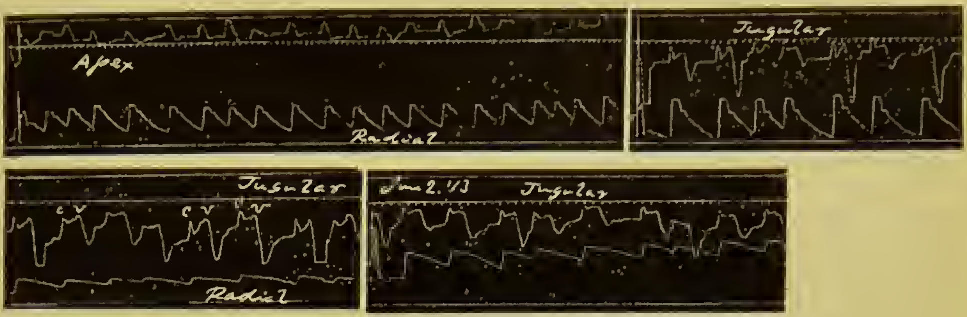

Fig. 2.—Tracings from James H.

TABLE 10.—Calorimetric Measurements in Case of James H.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.00	31.30	31.24	.....	2.17	31.07	30.98	23.3
2.02	31.25	31.17	23.1	2.18	31.055	30.97	....
2.03	31.23	31.16	.....	2.19	31.04	30.96	....
2.04	31.22	31.15	.....	2.20	31.03	30.955	23.4
2.05	31.20	31.13	23.3	2.21	31.02	30.95	....
2.06	31.19	31.12	.....	2.22	31.01	30.945	....
2.07	31.18	31.105	23.3	2.23	31.00	30.94	23.4
2.08	31.17	31.09	.....	2.24	30.995	30.93	....
2.09	31.15	31.08	23.2	2.25	30.995	30.925	....
2.10	31.13	31.06	.....	2.26	30.99	30.915	23.5
2.11	31.125	31.055	.....	2.27	30.98	30.90	....
2.12	31.11	31.05	23.2	2.28	30.975	30.895	....
2.13	31.10	31.04	.....	2.29	30.97	30.89	....
2.14	31.09	31.03	23.2	2.30	30.96	30.88	23.6
2.15	31.08	31.01	.....	3.21	30.395	30.34	....
2.16	31.07	30.99	.....				

The first examination of the hand flow was made on May 29, 1913. His hands were cold when he was brought into the room, having been exposed for some time near an open window. The day, however, was not especially cool. He was allowed to keep the hands wrapped up for twenty minutes in his gown before the observations were begun. Pulse 70 (sitting). The volume of the pulse seemed fair and was thought to indicate a much better flow than was actually shown by the examination, but the veins on the back of the hands, although prominent, filled but slowly when emptied of blood. Hands in bath at 1:50 p. m.; in calorimeters at 2:00½, and out of calorimeters at 2:30.

Cooling of calorimeters in fifty-one minutes, R., 0.565 degree; L., 0.54 degree. Volume of right hand 418 c.c., of left hand 396 c.c. The hands do not feel cold to the touch on coming out of the calorimeters. They are fairly red. The veins on the back of the hand and in the forearm are large, but fill with marked slowness on being emptied. Blood-pressure, left arm, systolic 136, 63 (sound gone). Another observation 134, 68. There was no sensible interval between the change in sound and its disappearance. A few of the larger beats were heard a little before the readings given as systolic pressure. The number of waves coming through increased as the pressure fell.

The flow in the hands in this examination works out at only 0.80 gram per 100 c.c. per minute for the right hand, and 0.64 gram for the left, for the last ten minutes of immersion in the calorimeters. If the whole period in the calorimeters is taken, the calculated flow is still less, as is always the case with a very small flow, the period required for the attainment of the steady state where the thermometers are changing uniformly being long.

A second examination on June 2, 1913, gave an even smaller calculated flow (0.40 gram per 100 c.c. per minute) for the last ten minutes in the calorimeters. The temperature readings followed precisely the same course as at the first examination. The question arises how such small flows can be reconciled with the fairly good volume of the arterial pulse at the wrist. The explanation is found partly in the fact that the venous return was hindered as indicated by the appearance of the veins. The increase in venous pressure while it did not hinder the conduction of the arterial pulse wave, apparently diminished the rate of translation of the blood. A second factor in the small flow was apparently a persistent local vasoconstriction in the hands. That this second factor was concerned is shown by the great improvement in the hand flow at the third examination, although the pulse-rate, far from being accelerated, was even slower than at the previous examinations.

Third examination June 16, 1913. He is feeling well, only weak. No dyspnea and no cough whatever. The day is very warm and the room temperature the highest in the whole series of observations. The veins on his hands and arms fill much more quickly after being emptied than on the two previous occasions. Amplitude of the pulse at the wrist is fair, but not strikingly greater than at the other examinations. Pulse 57 (sitting), with some irregularity but not so marked as before. Hands in bath at 4:06½ p. m.; in calorimeters at 4:15½, and out of calorimeters at 4:27.

Cooling of calorimeters in ten minutes, R., 0.045 degree; L., 0.04 degree. Volume of right hand in calorimeter 408 c.c., of left hand 392 c.c. Water equivalent of calorimeters with contents, R., 3,421; L., 3,409. Blood-pressure in left brachial, systolic 110, another observation 106, 80 (change in sound). Rectal temperature 37.6 C. (See Table 11.)

The general cutaneous vasodilatation at the third examination was evident and is doubtless related to the decidedly diminished systolic pressure. The hands shared in this general vasodilatation, and it is

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probable for this reason that the hand flow gives an index to the heart output. Since the hand flow with practically maximal vasodilatation is not half that of a young adult at this room temperature, the heart output is probably at most 50 per cent. of that of a healthy young adult. The three observations together show that in this man of 63 the range of the vasomotor adaptation of the hand blood-vessels is still considerable, a confirmation of his statement that the hot weather suited him.

TABLE 11.—Calorimetric Measurements in Third Examination of James H.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
4.15	31.45	31.50	.....	4.22	31.71	31.72	30.9
4.16	31.46	31.52	.....	4.23	31.765	31.76	....
4.17	31.49	31.54	.....	4.24	31.795	31.83	....
4.18	31.54	31.58	30.8	4.25	31.86	31.84	30.9
4.19	31.58	31.62	.....	4.26	31.89	31.87	....
4.20	31.62	31.655	30.9	4.27	31.925	31.90	....
4.21	31.67	31.69	.....	4.37	31.88	31.86	....

From the standpoint of the technic of the method it ought still to be mentioned that a local vasoconstriction so persistent as not to be overcome during the usual period of an examination (the disappearance of it being shown by a rather abrupt and henceforth steady rise of the thermometers) is rare in hospital cases, although in hands long exposed to cold it may be frequently met with. Where it exists the results cannot, of course, be used as average flows for the patient in question, although the intensity and persistence of the vasoconstriction may be of interest in relation to the patient's condition.

In a case of badly broken compensation in a boy (Joseph Z.), 16 years old, suffering from chronic endocarditis with aortic insufficiency and stenosis and mitral insufficiency, the flow in the right hand was 6.28 grams per 100 c.c. per minute, and in the left hand 4.79 grams. This is much too small for the age of the patient and the very high room temperature (28.1 C.). He was obviously in bad condition. Immersion of the left hand in cold water was followed by but a small diminution of the flow in the right, and immersion of the left hand in warm water by no increase at all, either because the dyspneic condition of the blood caused increased stimulation of the vasoconstrictors of the hand which the vasodilator effect of warmth to the contralateral hand could not overcome, or because the vasoconstrictor tone was already much diminished under the influence of the warm room, although, owing to the handicap of the heart, this was not shown in a large flow. Another possibility is that the dyspneic condition of the blood may have rendered the vasomotor centers less excitable to this form of afferent stimulation.

Joseph Z., boy aged 16, was admitted to the dispensary Nov. 11, 1910, suffering from aortic insufficiency and stenosis with attacks of acute pulmonary edema. He has had rheumatism for ten years. He was in the hospital three weeks for heart trouble which started four years ago. Has dyspnea and weakness. His heart is enlarged 16 cm. to the left, and 5 cm. to the right of the median line. Pulsation in the arteries of the neck. Apex beat heaving. Systolic impulse over apex. A systolic thrill can be felt to the right of the sternum. A double murmur over the apex and louder over the aortic region. Pulse 95. Moderate tension, rather slow rise and quick fall. Pistol shot in femorals. Capillary pulse.

Nov. 15, 1910, he was admitted to the hospital where he improved and after his discharge he remained well, keeping in bed, however, most of the time.

Feb. 2, 1911. When in the dispensary he had an attack of palpitation during which the pulse rate rose to 160, with great throbbing in the carotids and general cyanosis. He began to spit up pinkish frothy liquid. The attack lasted forty-five minutes. He was again admitted to the house, where the diagnosis of chronic endocarditis, mitral insufficiency and aortic insufficiency, was made. He suffered from occasional attacks of tachycardia and shortness of breath. The blood-examination showed hemoglobin 90 per cent. He was discharged July 5, 1911, "improved."

July 14, 1911, he had an attack in the dispensary. There was great pain referred to the right infrascapular region. He received morphin (grain ⅛) and atropin sulphate (gr. 1/300) hypodermically to relieve and calm him, and fifteen minutes later the blood flow in his hands was measured. Pulse (sitting) 140. Hands in bath at 3:01 p. m., in calorimeters at 3:11½. Mouth temperature 38.15 C. At 3:21 p. m. left hand was put into water at 8 C.

TABLE 12.—CALORIMETRIC MEASUREMENTS IN CASE OF JOSEPH Z.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
3:11	29.87	29.905	.....	3:27	30.59	
3:12	29.88	29.915	.....	3:28	30.60	Pulse 132.
3:13	29.91	29.93	.....	3:29	30.635	
3:14	29.98	29.97	.....	3:30	30.695	At 3:30 put left hand in water at 43 C.
3:15	30.07	30.04	28.1	3:31	30.735	
3:16	30.13	30.10	.....	3:32	30.775	Room 28.4 C.
3:17	30.21	30.13	.....	3:33	30.81	
3:18	30.22	30.15	.....	3:34	30.87	
3:19	30.27	30.20	.....	3:35	30.895	
3:20	30.29	30.22	.....	3:36	30.93	
3:21	30.32	30.235	.....	3:37	30.975	Room 28.3 C.
3:22	30.34	.....	.....	3:38	31.01	3:38 hand out calorimeter.
3:23	30.37	30.22	.....	3:38½		Temp. of L. 30.16 C.
3:24	30.40	.....	.....	3:48	30.97	Pulse 120. Mouth temp. 38.45 C.
3:25	30.49	.....	28.1			
3:26	30.54	.....	.....			

Cooling of calorimeters, R., 0.04 C. in ten minutes; L., 0.06 C. in fifteen one-half minutes. Volume of right hand 406 c.c., of left 412 c.c. He is right handed. Water equivalent of calorimeters with contents, R., 3,420; L., 3,425.

He attended from time to time at the dispensary feeling pretty well for awhile, but compensation broke down again and on March 3, 1913, he had again to seek admission to Lakeside Hospital with the cardiac dulness enlarged to the left to the mid-axillary line.

In another case of aortic stenosis and insufficiency and mitral insufficiency with fair compensation at the time of the blood-flow examination in a man (Matthew K.), 42 years old, the flow was 7.20 grams per 100 c.c. per minute in the right, and 5.49 grams in the left, with room temperature 22.5 C., a flow somewhat below the normal for his age and the external temperature, although by no means remarkably small. He had no edema and no dyspnea, but he complained of pain over the heart and was getting weaker.

Mat. K., aged 42, height 5 feet, 7 inches, weight 165 pounds, a worker in a railway shop, was admitted at the dispensary Dec. 2, 1910, suffering from aortic stenosis and insufficiency and mitral insufficiency. His illness began two months before and he has been getting worse ever since. He feels chilly at times. His weakness is increasing each day and he has had to give up work. He suffers from pain over the heart, palpitation and inability to sleep. There is a probable history of rheumatic fever seven years ago. The left border of the cardiac dulness is 12½ cm. to the left of the mid-sternal line, the right border 4 cm. to the right of it, upper border at third rib. No capillary pulse, no edema, urine normal.

The blood-flow in the hands was measured Jan. 24, 1911. He has no shortness of breath. The systolic blood-pressure is 170. Mouth temperature 36.6 C.; pulse (sitting) 80. Hands in bath at 3:16 p. m.; in calorimeters at 3:27, out of calorimeters at 3:42. There was 3,050 c.c. of water in each calorimeter. Room temperature 22.0 C. before the observations were begun.

TABLE 13.—Calorimeter Measurements in Case of Mat. K.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.26	29.42	29.19	.....	3.37	29.73	29.43	....
3.28	29.40	29.18	.....	3.38	29.78	29.46	....
3.29	29.42	29.18	.....	3.39	29.82	29.48	....
3.30	29.44	29.20	.....	3.40	29.86	29.51	....
3.31	29.47	29.21	.....	3.41	29.90	29.54	....
3.33	29.54	29.29	.....	3.42	29.96	29.58	23.1
3.34	29.60	29.33	.....	3.59	29.76	29.42	....
3.35	29.64	29.37	.....	4.04	29.70	29.37	....
3.36	29.70	29.40	.....				

Cooling of calorimeters in twenty-two minutes, R., 0.26 degree; L., 0.21 degree. Volume of right hand in calorimeter 440 c.c., of left 435 c.c. He is right handed.

He continued to come to the dispensary. On Feb. 2, 1911, he complained of pain over the precordia and down the shoulder and arm. His last visit was on April 2, 1913, when his condition was not essentially altered.

In a case of mitral and tricuspid insufficiency (P. B.) with venous engorgement, edema of the ankles and fluid in the peritoneal cavity, a perfectly good flow was seen in the hands (12.80 grams per 100 c.c. per minute for the right and 13.46 grams for the left, with room temperature 25.5 C.). A fair reflex vasoconstriction was obtained by the application of cold to the contralateral hand, but the application of warmth failed to increase the flow, even to the initial level, owing no doubt to the fact that the vessels were already so much dilated. There was no dyspnea during the experiment, and the driving power of the heart with its obviously powerful stroke was adequate to maintain a normal flow through the periphery. The vasomotor centers seem to have retained their normal excitability. The cord, therefore, in spite of the venous engorgement, was not suffering appreciably at the time.

P. B., section hand on a railway, aged 31, height 5 feet, 11 inches, was admitted to the dispensary May 12, 1911, with mitral and tricuspid insufficiency. He has been ill for eighteen or nineteen months, during which time he has been unable to work. He had acute articular rheumatism nineteen months before admission, had swollen feet, enlargement of the abdomen and palpitation of the heart and was in bed six weeks. The left border of the cardiac dulness is at the mid-axillary line. There is a large diffuse area of cardiac pulsation visible (positive systolic) and the framework of the chest undulates with each beat. Positive venous pulsation in both jugulars. Liver much enlarged with marked systolic pulsation. There is venous engorgement, edema of the ankles and fluid in the peritoneal cavity.

The blood-flow in the hands was measured May 12, 1912. There was no dyspnea during the examination. Pulse (sitting) 100. Mouth temperature 36.9 C. Hands put into bath at 2:29 p. m., into calorimeters at 2:39. At 2:50 p. m. left hand put into water at 8 C.

TABLE 14.—Calorimetric Measurements in Case of P. B.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
2:38	30.21	30.11	.....	2:57	31.67	
2:40	30.28	30.19	.....	2:58	31.71	
2:41	30.375	30.28	.....	2:59	31.77	
2:42	30.48	30.40	.....	3:00	31.82	Room 25.7 C.
2:43	30.59	30.495	.....	3:01	31.875	At 3:01 put left hand in water at 43.1 C.
2:44	30.68	30.61	25.5	3:02	31.91	
2:45	30.79	30.71	.....	3:03	31.97	
2:46	30.88	30.80	.....	3:04	32.02	Room 25.5 C.
2:47	30.97	30.875	.....	3:05	32.085	
2:48	31.06	30.96	.....	3:06	32.135	
2:49	31.14	31.06	25.6	3:07	32.195	
2:50	31.23	31.16	.....	3:08	32.26	
2:51	31.295	.....	.....	3:09	32.32	
2:52	31.345	.....	.....	3:10	32.38	3:10 hand out calorimeter.
2:53	31.395	.....	.....	3:10½	.....	Temp. of L. is now 30.98. Room 25.7 C.
2:54	31.475	.....	.....	3:22½	32.25	
2:55	31.545	.....	25.8	3:23½	.....	Temp. L. is now 30.88 C.
2:56	31.605	.....	.....			

Cooling of calorimeters, R., 0.13 degree in twelve one-half minutes; L., 0.28 degree in thirty-two minutes. Volume of right hand 510 c.c.; of left hand 480 c.c.

He entered Lakeside Hospital August 21, 1911. He had then neither cyanosis nor edema, but there was still fluid in the abdomen. The apparent incongruity between the distention of the abdomen, the pulsation of the liver and the great comfort of the patient was remarked. Heart dulness extends on the right to 7 cm.

from the mid-sternal line in the third interspace, on the left to the anterior axillary line in the sixth interspace. The blood examination showed 90 per cent. hemoglobin. He again entered Lakeside Hospital Nov. 2, 1911, and was discharged "improved" Feb. 20, 1912.

The large flow in P. B. contrasts with the small flow in Joseph Z., in whom the delivery of blood to the systemic vessels was seriously interfered with by the insufficiency of the aortic valve.

In Ernest M., another case of mitral insufficiency with chronic bronchitis, in a boy 14 years old, the flow was also good (12.74 grams per 100 c.c. per minute for the right hand and 12.45 grams for the left hand, with room temperature 23.4 C.). Compensation was so far established that he was able to come to the dispensary and had no dyspnea during the examination.

Ernest M., boy, aged 14, height 5 feet, 1¼ inches, was admitted at the dispensary Jan. 26, 1911, suffering from mitral insufficiency with chronic bronchitis. The fingers of both hands show well marked clubbing. He has had a cough ever since he was two years old. He still has the cough and is getting thinner. His arms are thin for his age. He gives a history of heart trouble. He has never been very strong and is not well enough to go to school. His appetite is good. Up to the present time there has never been any blood in the sputum, but on Feb. 7, 1911, he stated that since his last visit he spat some blood. The sputum examination was always negative as regards tubercle bacilli.

The hand flow was measured Jan. 26, 1911. Mouth temperature 38.2 C. Rectal temperature 38.5 C. Hands in bath at 2:56 p. m.; in calorimeters at 3:07, and out of calorimeters at 3:23. There was 3,150 c.c. of water in each calorimeter. Pulse (sitting) 116. The weather was mild with rain. Room 23.4 C.

TABLE 15.—Calorimetric Measurements in Case of Ernest M.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.06	29.71	29.68	.....	3.17	30.18	30.10	....
3.09	29.73	29.68	.....	3.18	30.24	30.16	23.4
3.10	29.77	29.72	.....	3.20	30.34	30.27	....
3.12	29.89	29.82	.....	3.21	30.40	30.33	....
3.13	29.96	29.89	.....	3.22	30.45	30.39	....
3.14	30.00	29.93	.....	3.23	30.50	30.42	23.1
3.15	30.06	29.99	.....	3.42	30.30	30.27	22.7
3.16	30.12	30.05	.....				

Cooling of calorimeters in nineteen minutes, R., 0.20 degree; L., 0.15 degree. L. was on the side of the room next to the radiator, though at a good distance from it. A small centrifuge had been started at 3:23 at the side of the room nearest to R. The difference in the rate of cooling of the calorimeters, which is decidedly greater than usual, may be thus accounted for. Volume of right hand 255 c.c., of left 240 c.c.

In another boy (Frank C.), 17 years old, with mitral stenosis and insufficiency, the flow was also quite normal in amount (11.25 grams for the right and 11.58 grams for the left hand, with room temperature 22.4

C.). Compensation was fairly established. The protocol has already been published.[6] Later he was admitted several times to Lakeside Hospital suffering from broken compensation and was discharged for the last time on March 4, 1912. He afterward died.

One of the most interesting cases was that of Albert H., since the heart underwent rapid deterioration within the period of the observations and the patient died soon after the last examination, when an autopsy was obtained. The patient was a man 31 years of age with a clinical diagnosis of mitral and tricuspid insufficiency, confirmed by the autopsy, which in addition showed pericarditis with large effusion into the pericardial sac. There was no doubt that the myocardium had suffered. The patient suffered much from dyspnea if he attempted to lie down. The flow in the right hand was 4.08 grams per 100 c.c. per minute, and in the left 4.54 grams, with room temperature 24.7 C., a distinctly subnormal flow. Reflex vasoconstriction of the hand was easy to obtain on immersion of the contralateral hand in cold water, but no reflex vasodilatation could be obtained, which agreed well with the obviously poor filling of the vessels of the hand. Ten days later he was again examined. The abdomen was now full of liquid, the legs and feet greatly swollen, the heart-sounds weak and the pulse at the wrists so weak that the heart-rate was counted with the stethoscope. The hands also had increased in size. The blood-flow in the hands was very small and what was considered significant at the time, less than half its amount at the last examination (2.0 grams for the right and 1.88 grams for the left). This was for a period of seven minutes, beginning fifteen minutes after insertion of the hands in the calorimeters. For the first fifteen minutes the flow was still less. The patient said he felt better, but the great decline in the blood-flow was remarked as an ominous symptom. He died in the hospital ten days after the last examination.

Albert H., colored hotel porter, aged 31, was admitted to the City Hospital April 3, 1912, complaining of dyspnea, cough and swelling of the extremities. He had rheumatism three weeks before admission and the legs were very painful. The edema and dyspnea began one week before admission. He has grown worse, coughs most of the time and is very tired on any exertion. The physical signs of fluid in the right pleural cavity are present. Heart dulness, upper border third rib, right border parasternal line, left border midway between nipple and anterior axillary line. The rate of the heart is rapid, the sounds feeble. There is a soft mitral systolic murmur with reduplication of the second sound. Radial pulse small and easily compressible. No fibrosis. Great edema of scrotum and prepuce, and edema of lower extremities. Albumin in urine. April 5 and April 7 the dyspnea and edema were less, the mitral murmur not so pronounced, the pulse soft and not well sustained. April 9, on which day the hand flow was first measured, the signs of an increase in the fluid in the right pleural cavity were present. The heart boundaries were the same as before and the edema was still considerable. Seven hundred and fifty c.c. of liquid was aspirated from the right thorax before the blood-flow examination. His maximum temperature on April 3 was 100.6 F. It rose gradually till April 9 when it reached 104.5 F. The systolic blood-pressure on April 5 was 152; April 7, 160; April 9, 160.

Hands in bath at 1:09 p. m., in calorimeters at 1:19. Mouth temperature 37.8 C. At 1:31 p. m. left hand put into water at 7.9 C.

TABLE 16.—Calorimetric Measurements in Case of Albert H.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
1:18	30.82	30.78	.....	1:35	31.13	
1:20	30.81	30.75	.....	1:36	31.14	
1:21	30.84	30.76	24.6	1:37	31.16	Room 24.7 C.
1:22	30.87	30.79	.....	1:39	31.19	
1:23	30.89	30.82	.....	1:40	31.195	At 1:40 left hand put in water at 43 C.
1:24	30.90	30.85	24.9	1:41	31.21	
1:25	30.96	30.90	.....	1:42	31.22	Room 24.8 C.
1:26	31.03	30.96	.....	1:43	31.23	
1:27	31.07	31.00	.....	1:44	31.245	
1:28	31.08	31.02	24.6	1:45	31.26	
1:29	31.085	31.04	.....	1:46	31.28	
1:30	31.095	31.07	.....	1:47	31.295	
1:31	31.09	31.09	.....	1:48	31.305	
1:32	31.10	.....	.....	1:49	31.325	
1:33	31.105	.....	24.5	1:50	31.33	1:50 hand out calorimeter.
1:34	31.115	.....	.....	1:59	31.23	Temp. of L. is 30.81 C. at 1:59.

Cooling of calorimeters, R., 0.10 degree in nine minutes; L., 0.28 degree in twenty-eight minutes. Volume of right hand 447 c.c., of left hand 450 c.c. He says he does most of his work left handed. Water equivalent of calorimeters with contents, R., 3,452; L., 3,455. Pulse (lying down) 120. Rectal temperature 39.1 C.

April 10 his maximum temperature was 103.8 F.; April 14, 103.3 F. April 17, "the dulness in the right thorax begins as high as the fifth rib posteriorly. Heart boundary is the same." Systolic blood-pressure April 16, 130; April 18, 140; April 19, 130.

Second examination of the hand flow, April 19, 1912. The abdomen now contains much liquid. The legs and feet are greatly swollen and he cannot sleep because he is unable to lie down on account of dyspnea. The heart-sounds are weak and the pulse at the wrist barely discernible. He says he feels better than before the tapping on April 9, but he seems worse than when examined after the tapping on that date. The arms and hands, according to his statement, are not swollen, but simply fat and there is no pitting. Yet measurement of the volume of the hands demonstrates an increase in their size, although the edema is not great enough to be detected by pitting. He has no fever now.

Hands in bath at 1:58 p. m.; in calorimeters at 2:09 p. m., and out of calorimeters at 2:45. At 2:35 the right hand was put into water at 42.7 C.

Cooling of calorimeters, R., 0.295 degree in twenty-eight and one-half minutes; L., 0.17 degree in eighteen and one-half minutes. Pulse 102 (counted with stethoscope). Rectal temperature 37.75 C. It was noticed that he now has piles. He never had them before. Volume of right hand in calorimeter 475 c.c., of left hand 505 c.c. Water equivalent of calorimeters with contents, R., 3,475; L., 3,499. (See Table 17.)

April 26, 1912, edema was general in the legs, arms and face. Maximum temperature 102.4 F. He died April 29. Results of necropsy: Pericarditis; 600 c.c. fluid in the pericardial sac. Mitral valve, edges thickened, insufficient. Tricuspid valve, insufficient. One thousand c.c. fluid in the abdomen. Chronic passive congestion of the liver, spleen and kidneys.

Whether the mere mechanical effect of the liquid in the pericardial sac contributed to the small flow in Albert H. at the second examination cannot of course be determined, although it is likely enough that this was a factor in addition to the weakening of the myocardium and the insufficiency of the valves. However, if the clinical diagnosis in the next case (Roman B.) be accepted, liquid may be present in considerable amount in the pericardial sac without reducing the hand flow very markedly. This patient was a man aged 22, in whom the diagnosis of mitral insufficiency and pericardial effusion was made. Blood-flow measurements in the hands were obtained on three occasions, the first on May 29, 1912, when the heart dulness was much diminished and the swelling of the legs present on admission had disappeared. The flow came out 7.61 grams per 100 c.c. per minute in the right hand and 10.59 grams in the left hand, with room temperature 22 C. He seemed fairly comfortable and had no dyspnea. On May 31, when the weather was warmer, the room temperature being 26.3 C., the flow was 8.76 grams for the right hand and 11.05 grams for the left. The average for the two hands is normal, or nearly so, and greater of course at the second examination, in accordance with the increased room temperature. He left the hospital, and after working in a foundry for two days, his legs became swollen and he had to return to the hospital on June 11 with the same

TABLE 17.—CALORIMETRIC MEASUREMENTS IN SECOND EXAMINATION OF ALBERT H.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.08	29.81	29.72	.....	2.28	29.66	29.59	....
2.10	29.74	29.67	.....	2.29	29.675	29.61	....
2.11	29.72	29.65	22.7	2.30*	29.685	29.62	....
2.12	29.705	29.635	.....	2.31	29.68	29.61	....
2.13	29.695	29.625	.....	2.32	29.69	29.625	....
2.14	29.69	29.62	.....	2.33	29.695	29.63	....
2.15	29.68	29.61	.....	2.34	29.70	29.63	....
2.16	29.67	29.60	22.5	2.35	29.705	29.635	....
2.17	29.665	29.595	.....	2.36	.....	29.63	....
2.18	29.65	29.58	.....	2.37	.....	29.635	23.5
2.19	29.64	29.575	.....	2.38	.....	29.635	....
2.20	29.635	29.565	22.6	2.39	.....	29.645	....
2.21	29.63	29.56	.....	2.40	.....	29.65	....
2.22	29.625	29.555	.....	2.41	.....	29.655	....
2.23	29.62	29.55	.....	2.42	.....	29.655	....
2.24	29.62	29.55	.....	2.43	.....	29.66	....
2.25	29.63	29.56	.....	2.44	.....	29.665	....
2.26	29.64	29.57	22.7	2.45	.....	29.67	....
2.27	29.65	29.58	.....	3.03½	29.41	29.49	....

* Here the bringing in of the warm water attracted his attention. In excitable patients this may cause a change in the flow.

symptoms of broken compensation which he had at first, dyspnea, cough, greatly increased area of cardiac dulness and the edema already mentioned. On June 13 his hand flow was again examined, and came out only 5.52 grams per 100 c.c. per minute for the right hand and 8.74 grams for the left, with room temperature 21.8 C., a considerable smaller flow than at the first examination, although the external temperature was practically the same. The flow, then, concomitantly with the cardiac breakdown, has been decidedly diminished. The marked inequality in the flow in the two hands persists throughout, although the relative difference is greater at the third than at the other two examinations. No local difference in the hands or arms could be discovered to account for the difference in the flows. It is possible that it is connected with intrathoracic changes not taken account of in the diagnosis. The question of differences of flow in the two hands associated with unilateral changes in the lungs and pleurae will be taken up in a future paper.

Roman B., a laborer, aged 22, was admitted to the City Hospital May 17, 1912. He had rheumatism for the first time three years before admission. He has a typical cardiorenal facies. He seems fairly comfortable, with no dyspnea. The heart presents a pear-shaped area of dulness, left border in the mid-axillary line, right border one to three fingers' breadth to the right of the mid-sternal line, making an obtuse cardiohepatic angle. The cardiac dulness is increased when he leans forward. There is a loud systolic murmur at the apex. The second sound in the pulmonic area is split. The sounds are distant. Pulse regular in rhythm, of fair volume, rather rapid rise, and well sustained. Liver three fingers' breadth below costal margin; hard, sharp edge, not tender. Edema of legs. Urine negative.

TABLE 18.—Calorimetric Measurements in Case of Roman B.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.21	31.03	31.05	21.4	3.32	31.52	31.68	....
3.23	31.08	31.09	.....	3.33	31.56	31.74	22.2
3.24	31.12	31.15	21.5	3.34	31.58	31.77	....
3.25	31.19	31.23	.....	3.35	31.60	31.825	22.6
3.26	31.23	31.315	.....	3.36	31.64	31.89	....
3.27	31.28	31.36	.....	3.37	31.68	31.94	22.8
3.28	31.30	31.42	.....	3.38	31.705	31.98	....
3.29	31.36	31.47	21.0	3.39	31.735	32.025	22.5
3.30	31.42	31.56	.....	3.52	31.555	.....	....
3.31	31.48	31.64	21.5	3.52½	.....	31.83	....

Cooling of calorimeters, R., 0.18 degree in thirteen minutes; L., 0.195 degree in thirteen one-half minutes. Volume of right hand 454 c.c. of left hand 439 c.c. He is right handed. Water equivalent of calorimeters and contents, R., 3,458; L., 3,446. Pulse (sitting) 96. Rectal temperature 37.95 C.

May 25, 1912, left cardiac border just outside the nipple line. Right border one finger's breadth outside of sternal margin. Cardio-hepatic angle less obtuse. Liver one finger's breadth below costal border. Heart sounds louder and more distinct.

May 29, 1912, the flow in his hands was measured. Hands in bath at 3:12 p. m.; in calorimeters at 3:21¾, and out of calorimeters at 3:39. Mouth temperature 37.25 C.

Second examination May 31, 1912. He says his right ankle pains him now. It was painful three years ago when he had rheumatism for the first time. Hands in bath at 1:51 p. m; in calorimeters at 2:01½, and out of calorimeters at 2:20.

The weather was considerably warmer than at the last examination.

TABLE 19.—CALORIMETRIC MEASUREMENTS AT SECOND EXAMINATION OF ROMAN B.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.01	31.04	31.03	26.2	2.12	31.52	31.65	26.2
2.03	31.04	31.06	.....	2.13	31.57	31.71	....
2.04	31.08	31.125	26.3	2.14	31.61	31.77	26.3
2.05	31.125	31.17	.....	2.15	31.67	31.85	....
2.06	31.20	31.25	26.4	2.16	31.72	31.925	26.3
2.07	31.27	31.34	.....	2.17	31.76	31.97	....
2.08	31.32	31.42	26.4	2.18	31.795	32.025	26.2
2.09	31.38	31.48	.....	2.19	31.83	32.08	....
2.10	31.42	31.54	26.3	2.20	31.88	32.13	26.2
2.11	31.48	31.60	.....	2.32	31.76	32.02	....

Cooling of calorimeters in twelve minutes, R., 0.12 degree; L., 0.11 degree. Volume of right hand 451 c.c., of left hand 445 c.c. Water equivalent of calorimeters with contents, R., 3,456; L., 3,451. Pulse (sitting) 87. Rectal temperature, 37.65 degrees.

June 12, 1912, he was readmitted to the hospital, complaining of precordial pain, dyspnea, and cough. The right leg pains him more than before. Lips cyanosed. Finger tips bluish. Edema in legs. There is a diffuse wave during systole not prominent in any one region. Limits of cardiac dulness were as follows:

Interspace	Supine Posture Distance in Cm. from Mid-sternal Line		Sitting Posture Distance in Cm. from Mid-sternal Line	
	Right Border	Left Border	Right Border	Left Border
6	9.5	16	12	17.5
5	8.0	15	9.5	15.5
4	6.5	10	6	11.0
3	4.0	7	..	....

Ausculation, with moderate pressure of stethoscope, rough systolic murmur at apex. Pulmonic second accentuated and split. Aortic second, weak. With pressure of stethoscope a soft blowing murmur is heard at apex during diastole. The sounds are reduced in intensity. Free fluid in abdomen.

June 13, 1912, third examination of the hand flow. Hands in bath at 1:58½ p. m.; in calorimeters at 2:09½, and out of calorimeters at 2:25.

TABLE 20.—CALORIMETER MEASUREMENTS IN THIRD EXAMINATION OF ROMAN B.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.09	31.145	31.06	21.4	2.20	31.345	31.47	22.0
2.11	31.13	31.07	.....	2.21	31.37	31.51	....
2.12	31.14	31.095	.....	2.22	31.385	31.545	....
2.13	31.165	31.13	21.8	2.23	31.395	31.59	22.1
2.14	31.18	31.17	.....	2.24	31.405	31.625	....
2.15	31.20	31.225	21.9	2.25	31.415	31.635	....
2.16	31.22	31.26	.....	2.34	31.28	31.51	....
2.17	31.26	31.325	22.0				
2.18	31.29	31.375	.....				
2.19	31.315	31.42	.....				

Cooling of calorimeters in nine minutes, R., 0.135 degree; L., 0.125 degree. Volume of right hand 451 c.c., of left 443 c.c. Rectal temperature 37.3 C. Water equivalent of calorimeters with contents, R., 3,456; L., 3,449.

In a case (Robert T.) diagnosed as pure aortic stenosis with perfect compensation in a man, aged 22 years, the average flow in the hands was at least equal to normal (10.45 grams per 100 c.c. per minute for the right hand and 13.97 grams for the left, with room temperature 20.3 C.). He entered the hospital not for his heart condition, but for surgical treatment.

Robert T., a railroad worker 22 years old, was admitted to the City Hospital Jan. 23, 1913, for surgical tratment (crushed toes on left foot). He had typhoid fourteen years ago; also rheumatism in the neck for several weeks when a child. Denies venereal diseases. For four years after typhoid had shortness of breath and still gets short of breath if he has to hurry up, especially if he changes the manner of his work, but not when he has become accustomed to a job and can work steadily without spurts. He is well-developed and well-nourished, no cyanosis. Boundaries of cardiac dulness one and a half finger's breadth to left of nipple line, right sternal border, third interspace. A blowing systolic murmur is heard over the entire area, but best in the aortic area where it is exceedingly

TABLE 21.—CALORIMETRIC MEASUREMENTS IN CASE OF ROBERT T.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Room C.
2.52	31.22	31.13	.....	3.00	31.38	31.42	20.3
2.53	31.19	31.10	.....	3.01	31.42	31.48	....
2.54	31.205	31.12	20.1	3.02	31.47	31.54	20.4
2.55	31.215	31.15	20.1	3.03	31.515	31.59	....
2.56	31.23	31.18	.....	3.04	31.56	31.65	....
2.57	31.27	31.24	20.2	3.05	31.595	31.71	20.4
2.58	31.30	31.29	20.3	3.06	31.64	31.77	....
2.59	31.35	31.36	.....	3.27	31.28	31.41	....

loud. From time to time the murmur disappears for one beat, the apex beat becomes weak and the radial pulse vanishes, the murmur corresponding to the next beat being very loud, and the apex beat very strong. The radial sphygmogram is the typical trace of aortic stenosis, with flat top and sloping up-stroke. The heart is slow. The radial pulse shows fair volume, but to appreciate this the artery must be in a particular position as the tension is low and the arm fat. The physical examination reveals nothing abnormal elsewhere. The flow in the hands were measured Jan. 31, 1913. Hands in bath at 2:41½ p. m.; in calorimeters at 2:52½, and out of calorimeters at 3:06. He sat during the whole examination with the injured left foot lying on a stool, the left leg horizontal and the right foot down. (Table 21.)

Cooling of calorimeters in twenty-one minutes, 0.36 degree for R. and L. Volume of right hand 458 c.c., of left 452 c.c. He is mostly right handed, he says. Water equivalent of calorimeters with contents, R., 3,461; L., 3,456. Blood-pressure, left arm, systolic 105 (palpation), 103 (stethoscope), 91 (sound sharply diminished), 87 (sound gone). Rectal temperature 36.6 C.

The last cases to be described are two of mitral stenosis and insufficiency, one with good (Mary S.) and the other with only slightly broken compensation (Frank W.) at the time of the examination. In the first case, a woman, 26 years old, the flow works out at 15.74 grams per 100 c.c. per minute for the right hand and 14.26 grams for the left. Even taking into account the relatively high room temperature (26.7 C.) and the youth of the patient, these flows are, if anything, above the normal.

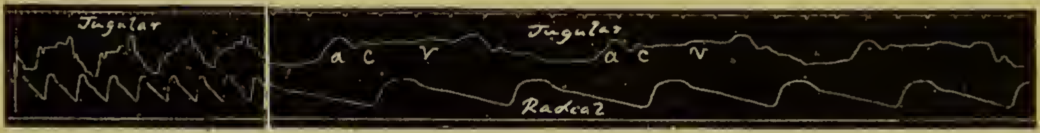

Fig. 3.—Tracings from Mary S.

When the blood-flow in the hands is not below the normal we are usually justified in assuming that the output of the ventricles is not less than normal. The large flow in this patient agrees well with the obviously exaggerated force of the ventricular stroke, and the absence of venous engorgement, of edema and of cyanosis. It confirms the conclusion that the increased respiratory rate at the time of the examination is a nervous affair not depending on deficient exchange in the lungs. Specimens of polygraph tracings are given in Figure 3. The *a* wave is prominent.

Mrs. Mary S., married woman, aged 26, a Hebrew, was admitted to the City Hospital May 29, 1913, complaining of pain in the chest, weakness and shortness of breath. Seven months before admission she had an attack of acute articular rheumatism and during this attack she began to have pain in her breast. Since then there have been several short periods during which she got short of breath. There seems, however, to be a strong neurotic element in the case, and she does not look particularly ill nor does she show any marked dyspnea. She is fat and well-nourished. No cyanosis, and little, if any, edema of the legs. No venous engorgement, no pulsation in the neck. The thorax is resonant throughout. The breathing everywhere vesicular. The apex beat is in the fifth interspace below the nipple; upper border of cardiac dulness in third interspace, right border, at right sternal margin; left border two finger's breadth out. Auscultation showed the signs of mitral stenosis and insufficiency. The rather rapid breathing appears to depend largely on nervous excitement. It is certainly not associated with any signs of deficient oxygen intake. The lips are red and she is even more comfortable lying down with her head on a single pillow than sitting up.

The blood-flow in the hands was estimated June 13, 1913. The day was rather warm (external temperature about 80 F). Hands in bath at 2:28 p. m., in calorimeters at 2:40 and out of calorimeters at 2:52. Mouth temperature (two observations) 36.6 C. Pulse (sitting) 84.

TABLE 22.—CALORIMETRIC MEASUREMENTS IN CASE OF MARY S.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Temp. Room C.
2.39	31.51	31.52	.....	2.47	31.86	31.81	26.7
2.41	31.55	31.57	26.4	2.48	31.90	31.84	....
2.42	31.60	31.60	.....	2.49	31.93	31.87	26.8
2.43	31.65	31.64	.....	2.50	31.97	31.90	....
2.44	31.71	31.68	26.5	2.51	32.01	31.94	....
2.45	31.76	31.73	.....	2.52	32.06	31.99	26.8
2.46	31.80	31.76	.....	3.07	31.89	31.83	....

Cooling of calorimeters in fifteen minutes, R., 0.17 degree; L., 0.16 degree. Volume of right hand 280 c.c., of left 259 c.c. She is right-handed. Blood-pressure, left arm, systolic 114, 95 (second phase), 62 (fourth phase), which was with practically no further fall in the pressure succeeded by the fifth phase (cessation of sound). Water equivalent of calorimeters with contents, R., 3,319; L., 3,302.

The last case is that of Frank W., a man 34 years old, with mitral stenosis and insufficiency with somewhat broken compensation, which was rapidly restored. Three examinations of the hand flow were made. The first on the day of admission, before any treatment had been given, showed a flow of 15.20 grams per 100 c.c. per minute for the right hand and 15.29 grams for the left, with the unusually high room temperature of 30.9 C. At the second examination, three days later, when the patient's clinical condition had improved, the flows were 11.95 grams for the right and 11.55 grams for the left hand, with the lower but still high room temperature of 28.5 C. The third examination, made six days after the second, with a room temperature (30.8 C.) the same as that during the first examination, showed a flow in the right hand of 11.44 grams per 100 c.c. per minute, and a flow in the left of 11.20 grams. The patient was feeling well. The re-establishment of compensation in this case was associated, then, with a diminution in the hand flow of 25 per cent. This diminution in the hand flow coincided with a reduction in the pulse-rate, quieter action of the heart and an improvement of the patient's clinical condition. It must be noted that the loss of compensation when the patient was admitted was not great, that his heart is permanently large and that there are no signs that the myocardium is, as yet, greatly impaired. The irregularity of the heart noted in the protocol is associated with premature auricular beats (Fig. 4). This condition is not included among the graver cardiac irregularities by those who have specially studied the clinical disorders of the mechanism of the heart beat. Loss of cardiac, or to speak more accurately, of cardiovascular compensation as expressed in an abnormal distribution of the blood, need not be always associated with a diminished flow through the periphery. Doubtless the abnormal distribution of the blood, resulting in engorgement of the venous side of the vascular system and a rise of venous pressure, is harmful, and is going eventually to cripple the machine. Yet it is not difficult to see that for a while the rate of the blood-flow through a part like a hand, far from being diminished, may be increased provided the driving power of the left ventricle, the aortic valves being intact, does not fail. For the rise of venous and therefore of capillary pressure may, up to a certain point, by increasing the caliber of the small vessels, favor the flow of blood. In order that this may result in increased flow through the part it is obvious that the arterial pressure must also be increased so that a sufficient slope may be maintained. And as a matter of fact, in Frank W., both the systolic and diastolic pressures in the brachial were materially higher at the first than at the second and third examinations. Corroborative evidence for the conclusion that some loss of compensation when the myocardium is not seriously affected is not incompatible for a time with a fully normal hand flow, is found in the observations on Mary S. and P. B., already referred to.

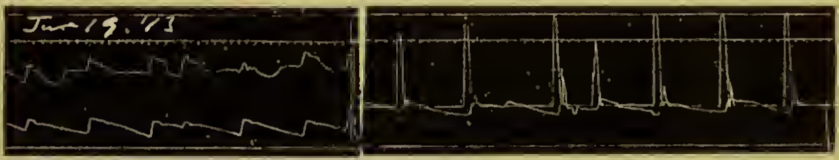

Fig. 4.—Tracings from Frank W. The left hand portion of the figure shows simultaneous tracings from the jugular bulb (upper trace) and the radial artery (lower trace). In the right hand portion of the figure simultaneous tracings from the apex (the large elevations) and the radial are given.

Frank W., an electrician aged 34, was admitted Feb. 9, 1912, to Lakeside Hospital. He says he never had rheumatism. His illness began six weeks before admission with pain all over, especially in the lumbar region and then in the epigastrium. In about a week shortness of breath came on and palpitation of the heart and he became blue in the face. A few days before admission edema was observed in the lower eyelids and the feet. The physical examination showed distended jugular veins with a systolic pulse. Heart: Apex beat in anterior axillary line in fifth interspace. Here there is a systolic impulse and thrill followed by a diastolic impact. A systolic impulse over the conus arteriosus. Left border of cardiac dulness is beyond the anterior axillary line, 18 cm. from the midsternal line, and the right border 9 cm. to right of midsternal line. The auscultatory signs are those of mitral stenosis and insufficiency. The pulse is irregular and arhythmic. Systolic blood-pressure 145, diastolic 108. Systolic pulsation of the liver. Liver dulness extends to umbilicus in right nipple line. Some edema of lower part of the back. Legs and feet edematous. When dependent, hands and feet are cyanotic. No clubbing of fingers. After a few days' rest the most prominent murmur became the presystolic rumble, heard best at the extreme apex, and indistinct elsewhere. The systolic sound was followed by a short blowing murmur, heard best to right of apex. The size and shape of the heart did not change materially. The edema rapidly disappeared. On March 6 the patient walked out of the hospital feeling well and with good cardiac compensation. The pulse rate which was 160 on admission gradually fell, and varied from 70 to 80 at the time of discharge. The minimum was 58. He broke down again after a time and was admitted to the City Hospital with the same symptoms and physical signs and was discharged improved. He was readmitted June 16, 1913. He worked for three days before he came in but was losing appetite and becoming short of breath. Some edema of the feet and ankles, but not a great deal. Slight cyanosis and dyspnea only on exertion. The point of the nose is red. The boundaries of the cardiac dulness are practically the same as those given in the physical examination at Lakeside Hospital. Pulsation in the neck veins.

The hand flow was measured June 16, 1913, a few hours after his admission and before he had had any drug treatment. The day was very warm. Pulse (sitting) 72, irregular. Hands in bath at 3:11½ p. m.; in calorimeters at 3:22¼, and out of calorimeters at 3:33.

TABLE 23.—CALORIMETRIC MEASUREMENTS IN CASE OF FRANK W.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3.22	31.49	31.49	.....	3.29	32.09	32.08	....
3.23	31.56	31.55	30.7	3.30	32.18	32.17	....
3.24	31.64	31.64	.....	3.31	32.27	32.255	....
3.25	31.72	31.72	30.8	3.32	32.355	32.34	31.0
3.26	31.82	31.82	.....	3.33	32.44	32.43	....
3.27	31.90	31.90	30.9	3.49	32.37	32.36	....
3.28	31.995	31.99	.....				

Cooling of calorimeters in sixteen minutes, 0.07 degrees.

Volume of right hand in calorimeter 456 c.c., of left hand 452 c.c. Water equivalent of calorimeter and contents, R., 3,460; L., 3,456. Blood-pressure in left brachial 133 (systolic), 103 (change in sound). Another observation 133 (systolic), 133 (change in sound). The pulse was slow and the sound diminished very rapidly to extinction after the change was heard. Rectal temperature 37.55 C.

Second examination June 19, 1913. He says he feels better. He has been receiving digitalis. There is no edema of the ankles, no dyspnea, no distention of the neck veins, no redness of the nose. The day was hot, but not so hot as that of the first examination. Hands in bath at 1:55 p. m.; in calorimeters at 2:10¼, and out of calorimeters at 2:24.

Cooling of calorimeters in twenty-three minutes, R., 0.18 degree; L., 0.16 degree. Radial pulse (sitting) 51. Volume of right hand in calorimeter 450 c.c., of left 439 c.c. Water equivalent of calorimeters with contents, R., 3,455;

L., 3446. Rectal temperature 37.75 C. Blood-pressure left arm, systolic 104, 84 (change in sound); the sound disappeared very soon after this reading. Another observation, systolic 108, 88 (change in sound followed almost at once by its complete disappearance). Pulse (sitting) 60, counted with stethoscope over apex beat. There is still arhythmia. On holding his breath the heart-rate suddenly increased considerably.

TABLE 23.—Calorimetric Measurements on Second Examination of Frank W.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.10	31.56	31.47	.....	2.18	32.09	32.02	28.3
2.11	31.61	31.53	.....	2.19	32.165	32.08	....
2.12	31.685	31.60	28.7	2.20	32.215	32.135	28.4
2.13	31.76	31.68	.....	2.21	32.295	32.20	....
2.14	31.83	31.745	28.6	2.22	32.33	32.255	28.4
2.15	31.895	31.82	.....	2.23	32.39	32.305	....
2.16	31.97	31.89	28.5	2.24	32.465	32.36	....
2.17	32.02	31.955	.....	2.47	32.285	32.20	....

Third examination, June 25, 1913. He feels well. Appetite fair, but does not sleep well. Since last examination the pulse-rate has varied between 60 and 72. The respiratory rate has rarely exceeded 20. The temperature has not exceeded 98.4 F. The day was very hot, about the same as the day of the first examination. He says his heart thumps much less than when he first came in although it gives an occasional thump. Hands in bath at 1:53 p. m.; in calorimeters at 2:04¼, and out of calorimeters at 2:19.

TABLE 24.—Calorimetric Measurements on Third Examination of Frank W.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
2.04	31.77	31.73	.....	2.13	32.32	32.26	30.85
2.05	31.78	31.74	.....	2.14	32.39	32.33	....
2.06	31.83	31.80	30.6	2.15	32.44	32.38	....
2.07	31.89	31.85	.....	2.16	32.50	32.44	30.85
2.08	31.975	31.935	30.8	2.17	32.565	32.49	....
2.09	32.04	31.995	.....	2.18	32.62	32.555	30.85
2.10	32.12	32.06	30.85	2.19	32.70	32.63	....
2.11	32.19	32.14	.....	2.35	32.62	32.555	....
2.12	32.26	32.20	.....				

Cooling of calorimeters in sixteen minutes, R., 0.08 degree; L., 0.075 degree. Volume of right hand in calorimeter 443 c.c., of left 432 c.c. Water equivalent of calorimeters with contents, R., 3,449; L., 3,440. Blood-pressure, left arm, systolic 104, 82 (change of sound followed very soon by its disappearance). Another observation. Systolic 109, 86 (change of sound). Pulse (sitting) 60, counted with stethoscope over apex. Respiration (sitting) 18. Rectal temperature 38.0 C.

SUMMARY

1. The smallest flows observed in the series of cases dealt with in this paper have been associated with marked irregularity of the heart, indicating involvement of the mechanism of the heart beat. In some of these cases the cardiac irregularity was associated with valvular lesions, but in those with the very poorest hand flows there was no evidence that the valves were involved.

2. Three cases were diagnosed as auricular fibrillation, all associated with mitral stenosis (and insufficiency). While the flow in all was below the normal it was decidedly greater in one of the patients than in the other two, although he was much the oldest of the three. This corresponded well with his clinical condition, which was good at the time of the examination, better than that of the other two patients. The ventricle in spite of its irregular action was on the whole beating fairly strongly, and was obviously delivering on the average of its beats, a fair amount of blood to the periphery.

3. In a case of mitral stenosis and insufficiency and tricuspid insufficiency, in which the heart showed marked arhythmia in part associated with the respiration (sinus arhythmia) the hand flow was also much below the normal.

4. Abnormally small flows were seen in a number of cases diagnosed as myocarditis with regular action of the heart, but feeble heart sounds not accompanied by murmurs.

5. In some cases diagnosed as myocarditis without valvular lesion, in which a serious clinical condition had previously existed, very fair hand flows, not much inferior to the normal, were found when the clinical condition had markedly improved.

6. In several cases of mitral insufficiency with good compensation and no signs of impairment of the myocardium, the hand flow was found to be quite up to the normal amount. In one case of mitral stenosis and insufficiency the flow appeared to be even somewhat greater than normal as if the big, well-compensated heart were discharging more than the usual quantity of blood.

7. In a case of mitral insufficiency with broken compensation, venous engorgement and edema, but no dyspnea or cyanosis, the hand flow was quite up to normal. In another case with the same lesions where there was little edema, no shortness of breath except on exertion, and none at the time of examination, the flow was also little if at all inferior to the normal flow, and the re-establishment of compensation was associated with an actual moderate diminution in the hand flow.

8. In a case of mitral insufficiency with physical signs of pericardial effusion a flow not much inferior to the normal was found after the patient had been some time in the hospital and had regained compensation, and when the heart dulness had decidedly diminished. When the patient, two days after leaving the hospital, broke down again and

TABLE 25.—DATA CONCERNING

Case	Age	Date	Pulse-Rate	Blood-Pressure	Temperature (C.) of				Volume of Hands in c.c.	
					Room	Art. Blood	Calorimeters			
							Right	Left	Right	Left
Jacob W..	59	5/ 1/11	100	190, (110)	25.0	37.1	29.92	29.93	508	486
					25.1	.....	30.16	.....	...	...
					25.1	.....	30.38	.....	...	...
James M..	60	6/27/12	87	152, 72	23.0	37.15	30.93	30.93	368	356
N. P.	27	5/12/13	70	95	23.8	36.3	31.44	31.33	298	276
Jacob S. ..	44	4/25/11	104	....	22.2	36.25	29.69	29.62	390	378
					22.6	.....	.....	29.76	...	....
					22.7	.....	.....	29.78	...	....
					22.7	.....	.....	29.83	...	....
T. F. K....	57	5/19/13	120	112, 58	24.0	36.85	31.76	31.75	444	458
Peter B....	59	4/21/11	80	....	24.5	36.45	30.17	30.14	360	320
					24.3	.....	30.50	.....	...	....
					24.3	.....	30.79	.....	...	....
Peter B...	......	5/17/11	84	....	26.6	36.5	30.63	30.43	410†	394†
					26.8	.....	30.80	.....	...	....
					26.8	.....	31.12	.....	...	...
					26.7	.....	31.46	.....	...	....
John T. ..	28	4/ 9/12	100	122	24.4	37.45	31.36	31.44	450	438
					24.3	.....	31.39	.....	...	....
James H. .	63	5/29/13	70	134, 68	23.4	36.1	31.00	30.92	418	396
Joseph Z..	16	6/16/13	57	110, (80)	30.9	37.1	31.69	31.74	408	392
		7/14/11	140	....	28.1	38.3	30.10	30.10	406	412
					28.2	.....	30.51	.....	...	....
					28.3	.....	30.85	.....	...	....
Mat K....	42	1/24/11	80	170	22.8	36.6	29.72	29.40	440	435
P. B.	31	5/12/11	100	....	25.5	36.9	30.76	30.68	510	480
					25.8	.....	31.55	.....	...	....
					25.5	.....	32.13	.....	...	....
E. M.	14	1/26/11	116	....	23.4	38.0	30.14	30.07	255	240
Frank C..	17	12/19/10	116	....	22.4	37.3	30.19	30.10	275	250
Albert H..	31	4/ 9/12	120	160	24.7	38.6	30.95	30.92	447	450
Albert H..		4/19/12	102	130	22.6	37.2	29.65	29.58	475	505
Albert H..		......	...	....	23.8	.....	.....	29.65	...	....
Roman B..	22	5/29/12	96	....	22.0	37.45	31.41	31.52	454	439
Roman B..		5/31/12	87	....	26.3	37.15	31.46	31.60	451	445
Roman B..		6/13/12	...	....	21.8	36.8	31.28	31.36	451	443
Robert T..	22	1/31/13	70	103, (91), 87	20.3	36.1	31.44	31.48	458	452
Mary S...	26	6/13/13	84	114	26.7	36.6	31.81	31.78	280	259
Frank W..	34	6/16/13	72	133, (108)	30.9	37.05	32.00	31.99	456	452
Frank W..		6/19/13	60	106, (86)	28.5	37.25	32.04	31.95	450	439
Frank W..		6/25/13	60	106, (84)	30.85	37.5	32.24	32.19	443	432

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* Good compensation.

† As his hands were short the marks were put higher up on the wrists than at the previous

‡ Badly broken compensation. The results on Stephen F., Mrs. A. and J. S. W. are sum-

Blood-Flow in Author's Cases

Heat Given Off in Gram-Calories			Blood-Flow in Gm. Per Min.		Flow Per 100 c.c. of Hand Per Min.		Notes
Right	Left	In Mins.	Right	Left	Right	Left	
1,050	801	13	12.50	9.55	2.46	1.96	Myocarditis.
1,225	....	10	19.62	.....	3.86	.....	Left hand in water at 42.9 C.
805	....	7	19.03	.....	3.75	.....	Left hand in water at 11.5 C.
366	270	10	7.32	4.82	1.99	1.35	Senile heart. Arhythmia.
283	216	11	5.88	4.39	1.97	1.59	Auricular fibrillation.
545	238	11	7.69	3.63	1.97	0.96	Auricular fibrillation.
....	170	5	.....	5.82	.....	1.54	Right hand in water at 43.3 C.
....	340	4	.....	14.59	.....	3.86	Right hand in water at 43.3 C.
....	340	5	.....	11.76	.....	3.11	Right hand dried and wrapped.
1,138	1,336	9	27.60	32.34	6.21	7.06	Auricular fibrillation.*
1,180	980	9	23.19	19.17	6.44	5.99	Myocarditis.
1,636	....	10	30.51	.....	8.47	.....	Left hand in water at 42.9 C.
913	....	7	25.62	.....	7.12	.....	Left hand in water at 8 C.
2,156	1,605	10	40.81	29.38	9.95	7.46	
924	....	5	36.03	.....	8.79	.....	Five min. just preceding vasomotor test.
1,643	....	10	33.93	.....	8.28	.....	Left hand in water at 8 C.
1,130	....	9	27.69	.....	6.75	.....	Left hand in water at 43 C.
516	396	10	9.41	7.32	2.09	1.67	Mitral insufficiency.‡
362	....	8	8.29	.....	1.84	.....	Left hand in water at 42.7.
154	119	10	3.35	2.55	0.80	0.64	Mitral stenosis, insufficiency; tricusp. insufficiency; arhythmia.
1,454	1,214	10	29.86	25.16	7.31	6.41	
1,505	1,165	8	25.50	19.75	6.28	4.79	Aortic insufficiency and stenosis.‡
1,402	....	9	22.22	.....	5.47	.....	Left hand in water at 8 C.
1,197	....	..	22.31	.....	5.49	.....	Left hand in water at 43 C.
2,159	1,704	11	31.70	23.90	7.20	5.49	Aortic insufficiency and stenosis.
3,608	3,618	10	65.29	64.63	12.80	13.46	Mitral and tricusp. insufficiency.
2,627	....	11	49.60	.....	9.72	.....	Left hand in water at 8 C.
2,102	.....	9	54.40	.....	10.67	.....	Left hand in water at 43.1 C.
2,988	2,772	13	32.49	29.88	12.74	12.45	Mitral insufficiency.
2,378	2,331	12	30.96	29.97	11.25	11.58	Mitral stenosis and insufficiency.
1,380	1,555	11	18.22	20.45	4.08	4.54	Mitral and tricusp. insufficiency.‡
452	455	7	9.50	9.48	2.00	1.88	
....	472	10	.....	6.94	.....	1.37	Right hand in water at 42.7 C.
3,008	3,970	16	34.58	46.49	7.61	10.59	Mitral insuff. with pericardial effusion.
3,440	4,176	17	39.5	49.18	8.76	11.05	
1,610	2,466	13	24.92	38.74	5.52	8.74	
2.007	2,626	10	47.85	63.15	10.45	13.97	Aortic stenosis.
2,091	1,763	11	44.09	36.94	15.74	14.26	Mitral stenosis and insufficiency.
3,152	3,148	10	69.35	69.11	15.20	15.29	Mitral stenosis and insufficiency .
3,280	3,146	13	53.80	50.73	11.95	11.55	
3,359	3,237	14	50.68	48.38	11.44	11.20	

examination.

marized in a previous paper (Heart, 1911, iii, 84).

returned with some dyspnea, cough and swelling of the legs, the hand flow was found distinctly below its previous value.

9. In two cases of mitral insufficiency with badly broken compensation, with venous engorgement, edema, cyanosis and dyspnea, the hand flow was much below the normal. In one of these cases a striking diminution occurred a few days before death.

10. In a case of apparently pure aortic stenosis with perfect compensation, the hand flow was normal in amount.

11. In a case of aortic stenosis and insufficiency, with mitral insufficiency, while there were no signs of broken compensation, the hand flow was somewhat below the normal.

12. In a case of aortic insufficiency and stenosis, with badly broken compensation (great dyspnea, pulmonary edema), the hand flow was greatly diminished.

While it is obvious that some of the groups of cases are much better represented in the observations than others, as is easily understood, since they had to be collected as chance offered, certain general conclusions which, although of course at present only provisional, are yet entitled to some weight, seem to emerge with sufficient clearness. It is scarcely necessary to say that in some points these conclusions simply confirm what is found by palpation of the radial pulse. But it is by no means true that even the qualitative result of the blood-flow measurement can always be predicted from feeling the pulse.

CONCLUSIONS

1. The hand flow is more apt to be markedly deficient in cases in which there is evidence of serious impairment of the myocardium, or more comprehensively and probably more accurately, of the mechanisms on which the force and rhythm of the heart's action depend, even when valvular lesions are absent, than in cases in which gross valvular lesions exist while the heart's action is strong and orderly. This holds even when in valvular diseases clinical signs of loss of compensation are present. In aortic insufficiency the hand flow appears to be less easily maintained at the normal level and more readily to fall below it when compensation is lost than in mitral insufficiency.

2. Even where there is considerable venous engorgement in cardiac cases the flow in the hands may be little if at all diminished, provided that the myocardium is not impaired. When in a case of broken compensation the flow in the hand remains good the reestablishment of compensation may be associated with a moderate decline.

3. When in a cardiac case with broken compensation the hand flow is normal or not much diminished, the indication is that the myocardium has not as yet suffered serious impairment. A decided diminution in the course of the case may be sigiificant of impending failure of the myocardium.

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STUDIES ON THE CIRCULATION IN MAN

XI. THE BLOOD-FLOW IN THE HANDS AND FEET IN CERTAIN DISEASED CONDITIONS OF THE VESSELS OR OF THEIR ~~VEN~~nervOUS MECHANISM *

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I. ARTERIOSCLEROSIS

It need scarcely be pointed out that several of the patients in the previous paper suffered from arteriosclerosis, in addition to valvular lesions of the heart or myocardial changes. In this section a few cases are brought together in which arteriosclerosis was pronounced and other lesions if present did not dominate the clinical picture. As a general result of the observations, it may be stated that in marked arteriosclerosis the flow in the hands is always smaller and the vasomotor reflexes weaker than in normal persons. Vasodilatation is easier to obtain by the application of warmth to the contralateral hand than vasoconstriction by the application of cold.

One of the purest cases of marked arteriosclerosis is that of Meyer G., a man aged 39, without detectable cardiac involvement. The flow was only 2.88 grams for the right hand and 3.46 grams for the left hand per 100 c.c. of hand per minute, with room temperature 22 C. An increase to 3.96 grams in the right was occasioned by immersion of the left hand in warm water, and the flow only fell to 3.52 grams when the left hand was subsequently put into cold water. It must not be forgotten, however, in connection with the small flow in this case that the man was a peddler accustomed to expose his hands in the open air in winter. Also he was a dispensary patient, and came from his work on a day in February.[1]

Meyer G., Hebrew peddler, aged 39, height 5 feet 6½ inches, was admitted at the dispensary Sept. 3, 1910, with marked arteriosclerosis. There was great thickening of all accessible arteries. The heart examination was negative in result. He complains of having had pain in the stomach during the past year. A test-meal showed free hydrochloric acid. No masses are palpable in the abdomen. He attributes his condition to strain in pushing heavy loads on his hand-cart. The hand flow was measured Feb. 3, 1911. He still complains of pain

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* From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University.

[1] See Paper IX of this Series, The Archives Int. Med., 1913, xii, 678.

in the epigastrium. On emptying capillaries on the back of the hand by pressure the color returns very slowly. Pulse, 72. Mouth temperature, 36.7 C. Systolic pressure in the right brachial, 110. Hands put into bath at 2:49 p. m.; into calorimeters at 2:59½.[2] Volume of right hand in calorimeter, 525 c.c.; of left hand, 525 c.c. He is right-handed. His hands are large. (Table 1.)

Another outside worker (John O'R.), a street laborer aged 60, with a diagnosis of arteriosclerosis and myocarditis, had a flow of 5.49 grams per 100 c.c. per minute in the right hand and 5.44 grams in the left hand with room temperature 23 C. The contralateral vasoconstriction to cold was slight, the flow in the right hand diminishing from 5.49 grams to 4.78 grams, but warmth gave a fair vasodilatation after the usual preliminary vasoconstriction. The protocol has already been published.[3]

TABLE 1.—CALORIMETRIC MEASUREMENTS IN CASE OF MEYER G.

Time	Right	Left	Notes	Time	Right	Notes
2:58½	29.74	29.81		3:28	29.98	
3:01	29.69	29.75		3:29	30.00	
3:02	29.70	29.74	Room temp. 22.2 C.	3:30	30.02	
3:03	29.70	29.74		3:31	30.07	At 3:31 left hand put in
3:04	29.70	29.74				water at 7.2 C.
3:05	29.70	29.75		3:32	30.09	
3:06	29.70	29.75		3:33	30.11	
3:07	29.69	29.76		3:34	30.13	
3:08	29.69	29.75		3:35	30.16	
3:09	29.69	29.75		3:36	30.18	
3:10	29.69	29.78	Room temp. 22.3 C.	3:37	30.20	Room temp. 21.9 C.
3:11	29.71	29.80		3:38	30.21	
3:12	29.72	29.81		3:39	30.22	
3:13	29.73	29.82		3:40	30.23	
3:14	29.75	29.85		3:41	30.25	
3:15	29.77	29.89		3:42	30.27	At 3:42 left hand dried and
3:16	29.78	29.90				wrapped in warm cloth.
3:17½	29.80	29.93		3:43	30.29	
3:19	29.82	29.97		3:44	30.31	
3:20	29.83	30.00		3:45	30.33	
3:21	29.86	30.01	Room temp. 21.7 C.	3:46	30.36	Room temp. 22 C.
3:22	29.88	30.03		3:47	30.39	
3:23	.....	30.08	At 3:23 left hand put	3:48	30.42	
			in water at 43 C.	3:49	30.45	Room temp. 22.2 C.
3:24	29.90	.....		3:50	30.48	At 3:50 hand out of calor.
3:25	29.92	.....		3:51	.....	Temp. of L. is now 29.75 C.
3:26	29.94	.....	Room temp. 21.6 C.	4:16	30.13	
3:27	29.96	.....		4:17	.....	Temp. of L. is now 29.48.

Charles S., a man aged 69, with sclerosed vessels, high blood-pressure and enlarged cardiac dulness, but no murmurs, had a flow in the right hand of only 5.25 grams per 100 c.c. per minute and in the left a flow of 5.01 grams, with the high room temperature of 28.3 C. The response of the vessels to reflex impulses from the contralateral hand was very poor, cold producing a small diminution in the flow, warmth no response whatever beyond the initial flow.

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[2] In all the observations unless otherwise stated the quantity of water in each hand calorimeter was 3,015 c.c.

[3] Cleveland Med. Jour., 1910, x, 385.

Charles S., a hammer man, aged 69, was admitted to Lakeside Hospital, June 26, 1911. He had gonorrhea forty-five years ago; never any chancre. He has been a heavy coffee and tea-drinker except in the last four or five years. He seldom drank whisky or beer, and smokes little. Six years ago following an attack of pneumonia he ate a heavy meal and immediately felt short of breath, dizzy and faint. He has had dizzy spells ever since. The attacks of dyspnea are worse at night and come on suddenly. Lately there has been swelling of the feet and ankles. There is Cheyne-Stokes respiration with periods of complete apnea lasting forty seconds. The anteroposterior diameter of the thorax is increased. There is difficulty in expelling air from the lungs. The cardiac dulness extends from 7 cm. to the right of the midsternal line in the fourth interspace to 14.5 cm. to the left of the midsternal line in the fifth interspace. The first sound at the apex is very tympanitic in quality with a slightly roughened element in it. Second sound normal, no murmurs or adventitious sounds. The blood-vessels are sclerotic. Pulse regular in rate and rhythm. The ascent is slow, no dicrotism. Blood-pressure: systolic, 180; diastolic, 120. Some edema of the skin of the genitalia and of the ankles is present. The skin is cool and dry. He has been on cardiac diet and treated with atropin and nitroglycerin. Hemoglobin, 95 per cent. Diagnosis, arteriosclerosis and myocarditis. He was discharged "improved," July 19, 1911.

TABLE 2.—CALORIMETRIC MEASUREMENTS IN CASE OF CHARLES S.

Time	Right	Left	Time	Right	Notes
2:45	.....	30.65	3:00	30.95	
2:46	30.61	.....	3:01	30.99	Room temp. 28.3 C.
2:47	.....	30.68	3:02	31.005	
2:48	30.67	.....	3:03	31.02	
2:49	.....	30.73	3:04	31.035	3:04 L. hand put in water at 43 C.
2:50	30.73	.....	3:05	31.055	Room temp. 28.3 C.
2:51	.....	30.77	3:06	31.09	
2:52	30.76	.....	3:07	31.11	
2:53	.....	30.825	3:08	31.125	
2:54	30.825	.....	3:09	31.135	
2:55	.....	30.87	3:10	31.155	
2:56	30.88	.....	3:11	31.20	At 3:11 hand out of calorimeter.
2:57	30.905	.....	3:12½	.....	Temp. of L. is now 30.76 C.
2:58	30.92	.....	3:29	31.08	Room temp. 28.15 C.
2:59	30.94	.....			

Cooling of calorimeters, R., 0.12 degree in eighteen minutes, L., 0.11 C. degree in seventeen and one-half minutes. Volume of right hand in calorimeter 437 c.c., of left hand 410 c.c.

The blood-flow in the hand was examined July 13, 1911. Mouth temperature, 36.3 C.; pulse (sitting), 80. Hands put into bath at 2:32 p. m.; into calorimeters at 2:44. At 2:55 p. m. left hand put into water at 8.5 C. Cooling of calorimeters, R., 0.12 degrees in eighteen minutes; L., 0.11 degree in seventeen and one-half minutes. Volume of right hand in calorimeters, 437 c.c.; of left hand, 410 c.c.

The last case to be referred to under this heading is that of Fred S., a man 58 years old, with pronounced arteriosclerosis of the vessels of the limbs, mitral insufficiency and pulmonary emphysema. The initial flow was 5.76 grams per 100 c.c. per minute for the right hand and 5.80 grams for the left hand, with an average room temperature of 23.8 C. Immersion of the left hand in warm water caused no change in the flow in the right for three minutes, an unusually sluggish reaction, but for the next ten minutes of immersion of the left hand in warm water the flow in the right rose to 7.69 grams per 100 c.c. per minute. Immersion of the left hand in cold water caused a reduction of the flow in the right to 3.65 grams per 100 c.c. per minute for the first three minutes, the flow then rising to 5.54 grams per 100 c.c. per minute for the next six minutes of immersion. When the left hand was again put into the warm water, there was only a small increase in the flow in the right (to 6.46 grams per 100 c.c. per minute for ten minutes' immersion).

TABLE 3.—Calorimetric Measurements in Case of Fred S.

Time	Right	Left	Room Temp. C.	Time	Right	Room Temp. C.	Notes
2:32½	31.09	31.07	....	3:00	31.78	....	
2:35	31.06	31.05	23.4	3:01	31.81	....	
2:36	31.07	31.05	....	3:02	31.855	24.0	
2:37	31.08	31.06	23.6	3:03	31.895	....	At 3:03 left hand put in water at 8 C. He feels it very cold and withdraws hand intermittently .
2:38	31.095	31.07	....	3:04	31.91	....	
2:39	31.11	31.08	....	3:05	31.92	23.9	
2:40	31.125	31.10	24.0	3:06	31.925	....	
2:42	31.17	31.15	....	3:07	31.95	....	
2:43	31.195	31.165	.....	3:08	31.975	24.0	
2:44	31.22	31.185	.....	3:09	31.995	....	
2:45	31.25	31.22	23.8	3:10	32.02	....	
2:46	31.29	31.26	.....	3:11	32.04	24.0	
2:47	31.32	31.29	.....	3:12	32.06	....	At 3:12 left hand put in water at 38.5 C.
2:48	31.36	31.34	23.9	3:13	32.085	....	
2:49	31.395	31.37	....	3:14	32.11	....	
2:50	31.425	31.40	.....	3:15	32.13	24.2	
2:51	31.45	.....	23.9	3:16	32.165	....	
2:52	31.48	.....	.....	3:17	32.195	....	
2:53	31.505	.....	.....	3:18	32.22	24.2	
2:54	31.54	.....	24.0	3:19	32.24	....	
2:55	31.59	.....	.....	3:20	32.27	....	
2:56	31.62	.....	.....	3:21	32.295	....	
2:57	31.66	.....	23.9	3:22	32.32	....	At 3:22 hand out of calor.
2:58	31.70	.....	.....	3:23	.....	....	3:23 Temp. of L. is 31.00 C.
2:59	31.74	.....	24.0	3:45	32.02	....	3:45 Temp. of L. is 30.79 C.

Fred S., a laborer, aged 58, was admitted to the City Hospital April 27, 1913, with marked arteriosclerosis, pulmonary emphysema and mitral insufficiency.

He complains of shortness of breath (asthma) which began in October last. He has not been able to work since. He says the condition seems stationary, neither improving nor growing worse. When he gets chilled an attack is brought on. The point of maximal cardiac impulse is 5 cm. outside the left nipple line. The greatest breadth of cardiac dulness extends at the sixth rib to the anterior axillary line; right border, right sternal margin. Roughened first sound at apex followed by systolic murmur, which is lost as the base is approached. Pulse fairly regular rhythm and rate, fair volume. Liver enlarged. Urine contains no albumin. A few hyaline and finely granular casts. Hot baths seemed to have a good effect on him.

The blood-flow in the hands was examined May 8, 1913. Hands in bath at 2:22½ p. m., in calorimeters at 2:33½. At 2:50 p. m. left hand put into water at 43 C. (Table 3.)

Cooling of calorimeters, R., 0.30 degree in twenty-three minutes, L., 0.61 degree in fifty-five minutes. Pulse (sitting) 116. Volume of right hand 497 c.c., of left hand 484 c.c. Rectal temperature 37.4 C. Water equivalent of calorimeters with contents, R., 3,492, L., 3,482. Blood-pressure left arm, systolic 126, 63 (sound gone). Another observation. Systolic 122, 101 (sudden diminution of sound), 63 (sound gone).

II. AORTIC ANEURYSM

If we leave out of account John M., a dispensary case who came in with cold hands on a winter day and could not wait for sufficient time to warm up and whose measured flow (3.96 grams per 100 c.c. per minute for the right hand) is therefore certainly too low,[4] a point of some consequence comes out in Table 19 in which the results are summarized; that is, that for the age of the patient and the temperature of the room the hand flow in these cases of thoracic aneurysm are either of the normal order of magnitude or at least not so conspicuously deficient as in those cases dealt with in Paper X, in which the stress of the pathological change falls on the myocardium rather than on the blood-vessels.

John M., an iron-molder, aged 32 years, weight 140 pounds, height 5 feet, 3½ inches, was admitted at the dispensary suffering from aortic aneurysm as shown by the Roentgen ray. He complains of pain over the sternum. Systolic blood-pressure, right arm 155, left arm 150. Blood-flow in the hands examined Feb. 13, 1911. Pulse (sitting) 72. Mouth temperature 37.0 C. Room temperature 22.2 C. His hands were cold when he came in. Right hand in bath at 2:56 p. m., in calorimeter at 3:07 and out of calorimeters at 3:36. At 3:25 left hand put into water at 8.5 C.

It is not, of course, suggested that in some of the cases of aneurysm deterioration and disordered function of the myocardium or crippling of the valves may not be of graver import than the aneurysm itself. But so far as the aneurysm, or rather the underlying condition which has occasioned the aneurysm has not led to deterioration of the heart, there is no reason in the mechanics of the circulation why the blood-flow through the hand should suffer. This is true even where the form of the pulse-wave may be greatly distorted by its passage through the aneurysmal sac. Of course, a sufficient degree of pressure of the sac on a subclavian artery or vein may diminish the flow in the corresponding hand. The great difference in the flow in the two hands in Paul K. may be accounted for by the pressure of the aneurysm on the left subclavian artery. The flow in his hands (for the last fifteen minutes in the calorimeters) was 7.64 grams for the right per 100 c.c. per minute and 5.9 grams for the left, with room temperature 22.6 C. (a ratio of 1.3 :1). For the right hand this flow is not markedly subnormal for his age. The diagnosis was auricular fibrillation with mitral insufficiency (and stenosis), well compensated at the time of the blood-flow examination and aortic aneurysm. There is no evidence that the aneurysm, unless by its mechanical pressure, caused any change in the flow.

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[4] The fact that immersion of the left hand in cold water caused only a very slight diminution in the flow in the right while immersion of the left hand in warm water increased the flow decidedly (to 5.5 grams) indicates that the vasoconstriction produced by the exposure of the hand to the cold was initially considerable.

TABLE 4.—CALORIMETRIC MEASUREMENTS IN CASE OF JOHN M.

Time	Right	Time	Right	Time	Right
3:06	29.15	3:19	29.28	3:29	29.47
3:10*	29.13	3:20	29.30	3:30†	29.48
3:11	29.14	3:21	29.32	3:31	29.50
3:12	29.14	3:22	29.33	3:32	29.51
3:13	29.16	3:23	29.36	3:33	29.54
3:14	29.19	3:24	29.38	3:34‡	29.58
3:15	29.21	3:25	29.40	3:35	29.62
3:16	29.23	3:26	29.42	3:36	29.67
3:17	29.24	3:27	29.425	3:53	29.49
3:18	29.27	3:28	29.44	3:55	29.47

* Room 22.0 C. † At 3:30 left hand dried and wrapped up. ‡ Room 22.4 C. Volume of right hand 380 c.c.

Paul K., a baker, 57 years old, was admitted to the City Hospital Feb. 21, 1912. There is a history of lues and of frequent acute attacks of articular rheumatism. A history of skin rash was obtained. He had gonorrhea ten or twelve times. His present illness began three weeks before admission. He had an attack of rheumatism at the time and began to be short of breath. His eyes have been swollen for three days. There is bulging over the heart. The thorax is barrel-shaped, and many dry râles can be heard. A loud systolic murmur can be heard over the apex, the heart is very irregular. Not all the heart-beats are felt at the wrist. Blood-pressure is 110 to 120. The Roentgen ray shows a marked prominence of the aortic arch on the left side and heart enlarged. He was put on digitalis. The pulse-rate, which was 132 on the morning after admission, fell rapidly. During March and April it varied between 75 and 90, his clinical condition improved and he was allowed to leave his bed and walk about the ward.

The blood-flow in the hands was examined April 24, 1912. Hands in bath at 1:32 p. m., in calorimeters at 1:42¾, and out of calorimeters at 2:06. (Table 5.)

Cooling of calorimeters in ten minutes, R., 0.13 degree; L., 0.12 degree. Volume of right hand 454 c.c., of left hand 451 c.c. He works mainly with his left hand although he is right-handed. Rectal temperature 38 C. Water equivalent of calorimeters with contents, R., 3,458; L., 3,456. After the examination it was noticed that the heart-rate was much increased (to 140 counted with a stethoscope) and that it was more irregular than before.

In Joseph C., a dispensary patient aged 50, with marked arteriosclerosis, a high systolic pressure (160 mm.) and distinctly dilated aortic arch, the flow was 6.69 grams for the right hand and 6.66 grams for the left, with room temperature 21.5 C. Considering the amount of arteriosclerosis and that in arteriosclerosis, as already stated, the hand flow has a tendency to be diminished, there is no evidence in this case that the presence of the aneurysm as such has reduced the flow.

Joseph C., an iron molder, aged 50, height 5 feet, 9½ inches, was admitted to the dispensary Jan. 30, 1911. He has been ill for six or seven years, during which time he has done no work. Six years ago he lost consciousness and after that his left arm was paralyzed. The grip of the left hand is weak, too weak, he says, to grasp objects; but on testing this the difference between the hands is not great. He gets very dizzy at times. There is much arteriosclerosis. He suffers from pain in the head, also in the breast and in the left hand. The Roentgen ray shows a definite dilatation of the arch of the aorta. Wassermann reaction negative on Feb. 6, 1911.

TABLE 5.—Calorimetric Measurements in Case of Paul K.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
1:42	31.13	31.29	....	1:56	31.40	31.465	....
1:44	31.07	31.21	....	1:57	31.45	31.50	....
1:45	31.08	31.21	22.8	1:58	31.49	31.525	22.6
1:46	31.095	31.225	....	1:59	31.51	31.53	....
1:47	31.11	31.23	....	2:00	31.56	31.58	....
1:48	31.13	31.25	22.8	2:01	31.605	31.61	....
1:49	31.165	31.29	....	2:02	31.65	31.635	....
1:50	31.19	31.31	....	2:03	31.70	31.67	....
1:51	31.21	31.32	....	2:04	31.75	31.71	22.6
1:52	31.25	31.35	....	2:05	31.795	31.75	....
1:53	31.29	31.38	22.9	2:06	31.83	31.76	....
1:54	31.32	31.41	....	2:16	31.70	31.64	....
1:55	31.37	31.43	....	....	.....	.....	....

The hand flow was examined on Jan. 31, 1911. Hands in bath at 2:52 p. m., in calorimeters at 3:05, and out of calorimeters at 3:20; 3,056 c.c. of water in each calorimeter. Pulse (sitting) 88. Mouth temperature 37.2 C. (Table 6.)

Cooling of calorimeters, R., 0.19 degree, and L. 0.16 degree in fourteen minutes. Volume of right hand 505 c.c., of left 480 c.c. Blood-pressure, systolic in right brachial 160, in left brachial 164.

In William B., a man aged 53, suffering from thoracic aneurysm, the flow in the right hand was 8.38 grams per 100 c.c. per minute and in the left 7.33 grams with room temperature 20.8 C. (for fourteen minutes in calorimeters). The systolic pressure was very high (205 mm.). He was still taking nitroglycerin at the time of the blood-flow examination.

A second examination made at the dispensary nearly four weeks later showed a flow of 10.23 grams per 100 c.c. per minute for the right and 9.47 grams for the left hand, with room temperature 22.2 C. These flows are certainly not small for a man of his age and with sclerosed arteries. The inequality in the flow in the two hands is no greater than may be seen in normal persons, and it will be observed that the ratio between the flows in the two hands is the same at the two examinations (1:1.08).

TABLE 6.—Calorimetric Measurements in Case of Joseph C.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3:04	29.13	29.12	20.3	3:16	29.55	29.51	....
3:06	29.11	29.10	....	3:17	29.61	29.53	21.5
3:07	29.14	29.11	....	3:18	29.67	29.62	....
3:08	29.18	29.12	21.5	3:19	29.72	29.67	....
3:09	29.20	29.14	....	3:20	29.78	29.71	....
3:10	29.25	29.19	....	3:32	29.61	29.58	....
3:11	29.29	29.22	....	3:34	29.59	29.55	....
3:12	29.34	29.31	....	....	.....	.....	....
3:13	29.39	29.33	21.4	....	.....	.....	....
3:14	29.45	29.39	....	....	.....	.....	....
3:15	29.51	29.43	....	....	.....	.....	....

TABLE 7.—Calorimetric Measurements in Case of William B. First Examination

Time	Right	Left	Time	Right	Left
2:37	28.38	28.54	2:48	28.70	28.82
2:40	28.34	28.53	2:51	28.90	29.00
2:42	28.39	28.58	2:53	29.04	29.11
2:43	28.43	28.61	2:55	29.20	29.22
2:45	28.56	28.70	2:56	29.27	29.28
2:46	28.61	28.75	3:12	29.09	29.10

William B., a man aged 53, height 5 feet, 2 inches, weight 152 pounds, had an aneurysm of the thoracic aorta involving the innominate also to some extent. After being under observation at the dispensary for a considerable time he was admitted to Lakeside Hospital where he was under treatment for a month (digitalis and nitroglycerin). His hand flow was examined at the time of his discharge from the hospital. He felt much better than when he entered, on Dec. 22, 1910. He has no cough but there is a history of cyanosis, although there is no cyanosis now. He says his hands always feel rather cool, especially when his heart is bad.

Hands in bath at 2:26½ p. m., in calorimeters at 2:38½, and out of calorimeters at 2:56; 3,050 c.c. of water in each calorimeter. Room temperature 20.4 C.

Room temperature at end of observations 21.2 C. Volume of right hand in calorimeter 410 c.c., of left hand 390 c.c. Cooling of calorimeters in sixteen minutes 0.18 C. degree. Pulse (sitting) 84. Mouth temperature 37.1 C. Water equivalent of calorimeters with contents, R., 3,458; L., 3,442. (Table 7.)

The second examination was on Jan. 17, 1911. He says he feels about the same as at the first examination, only the shortness of breath on exertion is greater. Systolic blood-pressure 210. Hands put into bath at 3:09 p. m., in calorimeters at 3:21, and out of calorimeters at 3:37; 3,050 c.c. of water in each calorimeter. Room temperature 22.2 C.

TABLE 8.—Calorimetric Measurements in Case of William B. Second Examination

Time	Right	Left	Time	Right	Left
3:19	30.70	30.49	3:31	31.13	30.86
3:23	30.69	30.48	3:32	31.19	30.91
3:25	30.79	30.57	3:33	31.23	30.94
3:26	30.86	30.62	3:34	31.29	31.00
3:27	30.92	30.67	3:35	31.34	31.07
3:28	30.97	30.71	3:36	31.39	31.11
3:29	31.02	30.77	3:37	31.44	31.16
3:30	31.07	30.81	4:00	31.12	30.85

Cooling of calorimeters in twenty-three minutes, R., 0.32 C. degree; L., 0.31 C. degree. Volume of right hand in calorimeter 435 c.c., of left 410 c.c. Mouth temperature 36.9 C. Water equivalent of calorimeters with contents, R., 3,478; L., 3,458. Pulse (sitting) 88.

In Richard B, a man aged 38, with a large aortic aneurysm extending, as shown by the Roentgen-ray, to a considerable distance to the right of the sternum, there was a decided deficiency in the flow of the left hand as compared with the right (10.91 grams per 100 c.c. per minute for the right, 8.15 grams for the left, a ratio of 1.33 :1). For the room temperature of 28 C., 10.9 grams is not a large flow, but neither is it decidedly small. The vasomotor reflexes from the right to the left hand were normal in direction, and not strikingly deficient in intensity, showing that the chief afferent path in the vasomotor reaction to warmth or cold (the nerves of warmth and cold sensation) have not appreciably suffered by stagnation of the circulation due to the pressure of the aneurysm on the right subclavian vein. Now, when pressure is maintained on the arm at a level somewhat below the systolic arterial pressure by means of the cuff of a sphygmomanometer the warmth sensation suffers early, so that it is impossible to appreciate the contact of a warm tube, while the sensation of pain is at this stage less affected. As has been pointed out in Paper X, a certain amount of venous distention, provided that the arterial pressure is correspondingly increased, may even be associated with an increased flow, because of the increased cross-section of the smaller vessels. So far as the arterial path to the right arm in Richard B. is concerned, the conditions would favor a greater flow in the right hand, for as shown at the necropsy the aneurysm provided a much wider entrance than normal for the blood going to the right subclavian and possibly a reservoir which helped to maintain the flow during diastole.

Richard B., a colored gardener, aged 38, height 5 feet, 7½ inches, was admitted to Lakeside Hospital May 22, 1911, with an aneurysm diagnosed as aortic. He complains of hoarseness during the past two weeks and vomiting during the past week, also cough. He admits lues. There is a tender pulsating mass in the suprasternal notch with fulness in the right supraclavicular region. Heart 3 cm. to left of nipple. A distant systolic murmur at the supraclavicular notch. The aortic second is slightly accentuated. There is distinct diastolic shock, unilateral (right) distention of veins, and clubbing of fingers. The Roentgen ray shows an enormous shadow upward and to the right. The patient continued in the hospital until his death, Aug. 22, 1911. There was no right radial pulse for the last week of life. Blood examination on May 23, 1911, showed hemoglobin 95 per cent., leukocytes 5,000. June 1 the Wassermann test was strongly positive. The necropsy showed a saccular, spherical aneurysm of the innominate artery 3 to 4 inches in diameter. The arch of the aorta was not involved except for the somewhat enlarged ring at the beginning of the innominate opening into the sac.

Hand flow examined May 23, 1911. Pulse (sitting) 100. Mouth temperature 37.1 C. Hands put into bath at 2:44 p. m., into calorimeters at 2:54½. At 3:08 p. m. right hand put into water at 8.1 C.

TABLE 9.—Calorimetric Measurements in Case of Richard B.

e	Right	Left	Room Temp. C.	Time	Left	Room Temp. C.	Notes
	30.43	30.38	....	3:13	31.225	....	
	30.475	30.42	27.7	3:14	31.28	....	
	30.53	30.43	....	3:15	31.325	28.0	
	30.595	30.46	....	3:16	31.36	....	At 3:16 put right hand in water at 43 C.
	30.695	30.525	....	3:17	31.38	....	
	30.78	30.60	....	3:18	31.415	....	
	30.86	30.63	....	3:19	31.46	....	
	30.935	30.69	27.9	3:20	31.525	28.3	
	31.02	30.74	....	3:21	31.58	....	
	31.12	30.825	....	3:22	31.625	28.2	
	31.20	.....	....	3:23	31.67	....	
	31.295	30.93	....	3:24	31.725	....	
	31.34	30.98	....	3:25	31.80	....	
	31.395	31.02	....	3:26	31.85	28.2	Hand out of calorimeter.
	31.46	31.035	....	3:41	31.75	28.0	Temp. of R. is now 31.27 C.
	.....	31.07	28.0				
	.....	31.10	....				
	.....	31.125	....				
	.....	31.155	....				

Cooling of calorimeters, R., 0.19 degree in thirty-three minutes; L., 0.10 C. degree in fifteen minutes. Volume of right hand 495 c.c.. of left 437 c.c. There is an obvious difference in the size of the two hands. He is right-handed.

The next case, that of Samuel S., a man 31 years old, illustrates the fact that even very marked differences in the form of the radial pulse on the two sides, differences perfectly evident both to the finger and on the sphygmogram, may be associated with a comparatively small difference in the flow in the two hands. The right radial showed a typical pulse of aortic insufficiency with abrupt ascent to a sharp apex and abrupt fall, while the left radial gave a sphymogram with a rounded apex. The blood-pressure in the two brachials was also quite different, the systolic pressure being 157 in the right and 118 in the left. The physical signs of aortic insufficiency were present.

The blood-flow measurement showed a difference no greater than may be seen in normal persons between the two hands (11.11 grams per 100 c.c. per minute for the right and 10.32 grams for the left, with room temperature 22.2 C.), a perfectly normal flow for a man of this age. The conclusion was drawn that the aneurysm in distorting the form of the pulse-wave did not interfere materially with the free passage of blood through the left subclavian artery. The man died the same night about five hours after the examination by a rupture of the aneurysm into the left bronchus. It is worthy of remark that five hours before his death the blood-flow in his hands, which no doubt in this case was an index of the output of his heart, was quite normal. He was to die, not because his heart was failing, but because the wall of the aneurysmal sac had been thinned to the bursting point. A very different tale would have been told by the hand flow in a case of impending heart-failure as in Stephen F., or Albert H. (Paper X), or Anthony P.

Samuel S., a colored music teacher, aged 31, was admitted to the City Hospital Dec. 7, 1912, with thoracic aneurysm. He is a well-developed man 5 feet, 10½ inches tall, weight 160 pounds. He has had spells of intense dyspnea for the past six weeks. He has been continually getting worse to the present time, is much cyanosed, and suffers much from cough which he has had from the age of 16. He has smoked cigarettes to excess, and also has used a good deal of alcohol. He denies lues although he admits the possibility of it.

The left pupil is smaller than the right and does not react to light or accommodation. There is diffuse pulsation of the lower third of the neck. Tracheal tug is present. The left side of the thorax moves less than the right. The percussion note is dull over the entire left side [compression of the left lung by the aneurism(?)]. Over the left lung the breath-sounds are very faint, distant and bronchial in character. The cardiac dulness at the level of the second rib extends three fingers' breadth to the right of the right sternal border and the same distance to the left of the left sternal border. In the fourth interpsace it extends from two fingers' breadth to the right of the right sternal border to the left midaxillary line. The apex beat is visible and palpable in the sixth interspace, two fingers' breadth outside the nipple line. Systolic and presystolic thrills are palpable over the apex. Loud booming systolic and diastolic murmurs are heard at apex. Loud presystolic murmur followed by systolic murmur is heard over aortic and pulmonic areas. The sternum rises fully a half-inch with each systole. The radial pulse is regular, rhythmical, asymmetrical, the sphygmogram of the left radial having a rounded apex, and that of the right a sharp (aortic insufficiency) apex. The pulse is synchronous in the two radials and of good volume and tension. The difference in the form of the pulse-wave is very evident to the finger.

The blood-flow in the hand was measured Dec. 10, 1912. Hands in bath at 1:50 p. m., in calorimeters at 1:59½, and out of calorimeters at 2:13 p. m.

TABLE 10.—Calorimetric Measurements in Case of Samuel S.

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
1:59	31.40	31.43	....	2:07	32.11	32.13	22.25
2:00	31.435	31.49	22.4	2:08	32.195	32.20	....
2:01	31.55	31.58	22.4	2:09	32.27	32.265	22.2
2:02	31.64	31.68	....	2:10	32.35	32.36	22.1
2:03	31.74	31.78	22.3	2:11	32.395	32.42	....
2:04	31.85	31.88	....	2:12	32.47	32.465	22.3
2:05	31.94	31.95	....	2:13	32.53	32.53	....
2:06	32.01	32.055	22.3	2:41	32.17	32.17	....

Cooling of calorimeters in twenty-eight minutes, 0.36 degree. Volume of right hand 580 c.c., of left hand 603 c.c. Water equivalent of calorimeters with contents, R., 3,559; L., 3,577. Rectal temperature 38.4 C. Blood-pressure left arm, systolic 118, 58 (sound suddenly diminished); right arm, systolic 157, 61 (sound abruptly diminished). Another observation on the right arm gave identical results. Three days previously, according to another observer, the pressures were 160 (systolic), 45 (change of sound) in the right, and 130, 55 in the left brachial.

A necropsy was performed by Dr. A. A. Johnson, Pathologist at the City Hospital, to whom I am indebted for the following details. Heart, left ventricle dilated moderately, average thickness 16 to 18 mm. Other cavities normal. The segments of all the valves except the aortic are normal and the orifices are not dilated. The aortic ring in the formaldehyd-preserved specimen measured 8 cm. The aortic valve segments are slightly thickened and curled along their free edges. The openings of the coronary arteries are free and of the usual size. The aorta immediately above the aortic ring is smooth and free from thickening. Opening from the anterior aspect of the transverse arch is a large sacular aneurysm adherent to the sternum. The sac is oval, 10 by 8 cm. in diameter. The walls are thin (2 to 4 mm.) and are quite free from fibrin. The opening from the aorta into the sac measures 5 by 3.5 cm. The innominate opens by a somewhat dilated mouth posterior and external to the opening into the aneurysm and situated opposite the middle of the latter opening. The left common carotid and subclavian arteries come off from the aorta about 1 cm. beyond the upper border of the opening between the aorta and the aneurysm. Rupture in the sac on the inferior surface has irregular edges and measures 3 by 1 mm., leading into the left bronchus 1 cm. from the bifurcation.

It will be seen that there was no stenosis of the orifice of the left subclavian, but its origin was situated distal to the orifice of the aneurysmal sac, while the origin of the innominate was directly opposite the center of that orifice. The direction of the opening of the innominate was such that the blood coming from the heart would pass straight into it, all the more as the opening of the innominate was somewhat dilated. This would account for the abrupt rise in the sphygmographic curve and the high maximum pressure in the right arm. The sudden fall in the sphygmogram if partly due to actual regurgitation through the aortic orifice, was probably due still more to the effect of rapid expansion of the thin aneurysmal sac, which after closure of the aortic valve would still go on yielding and so exert a suction action, especially on the orifice of the innominate placed directly opposite it. On the other hand, the action of the large aneurysmal sac lying proximal to the left subclavian would be to damp the pulse-wave in that artery and delay the arrival of the crest. This would not necessarily affect the total flow, the pulsatory element in which is measured not by the absolute height of the crest, but by the area enclosed between the sphygmogram and the line of diastolic pressure.[5]

The last case included in the group of aneurysms (that of John McL.) is the only one which shows a notably small hand flow. It is placed in this group merely to emphasize the point that in drawing any general deductions from such measurements the proper classification of the cases is of great importance.

John McL., a plasterer, aged 50, height 5 feet, 11½ inches, was admitted to the City Hospital July 6, 1912, with general edema (in face, hands, arms, legs and feet), also cyanosis in the lips and fingers. He complains of "kidney trouble." He looks anemic. The heart shows an impure first sound at the apex. The aortic second is greatly accentuated, the blood-pressure is high (systolic 200). The abdomen is distended with free fluid. Albumin and casts were present in the urine all along. On July 11 about 7 liters of fluid was removed from the abdomen. There was no detectable fluid in the thoracic cavity. A diagnosis of hepatic cirrhosis was made. Aug. 19, 7,080 c.c. of fluid was removed from the abdomen.

On Aug. 27, 1912, the hand and foot flows were estimated and found exceedingly small (0.41 gram per 100 c.c. per minute for the right hand and 0.57 gram for the left hand, with room temperature 22.2 C.; 0.17 gram per 100 c.c. per minute for the right foot and 0.14 gram for the left foot, with room temperature 21.2 C.).

Aug. 28, 1912, 1,965 c.c. of liquid was taken from the abdominal cavity at 1:30 p. m., and the hand and foot flows were again measured. They were larger than on the previous day, but still quite small (1.11 grams per 100 c.c. per minute for a period of seventeen minutes for the right hand and 1.18 grams for the left hand, with room temperature 21.1 C.; 0.66 gram per 100 c.c. per minute for the right foot for the last ten minutes of a period beginning twenty minutes after insertion of the feet into the calorimeters, and 0.65 gram for the left foot). The ratio between the flows in the feet and hands (1:1.75) is near enough the normal to permit the conclusion that the small flow in both has a common cause. The presence of an aneurysm of the aorta was not diagnosed during life. The small blood-flow in the hands has certainly nothing to do with the existence of the aneurysm. It is without doubt dependent on the cardiorenal, or cardiorenalhepatic affection, that is to say, on such factors as the vasoconstriction of which the high blood-pressure is one expression, on the coincident anemia, and on the crippling of the heart muscle. The small flow in the feet may also depend in part on the mechanical hindrance imposed by the fluid in the peritoneal cavity or in the connective tissue of the legs. But if this were an important factor the ratio of hand to foot flow would be disturbed.

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[5] Paper V of this series, The Archives Int. Med., 1912, ix, 706.

The patient died Dec. 27, 1912. The necropsy showed general peritonitis, aneurysm of the descending thoracic aorta, cloudy swelling and parenchymatous change in the kidneys. The pericardium was adherent to the left pleura, but not to the epicardium. The heart was pale (weight 300 grams), with some dilatation and hypertrophy of the left ventricle. The mitral orifice was dilated and the edges of the mitral valve were thickened and puckered. The edges of the aortic valve were thickened and slightly curled. The sinuses of Valsalva were dilated. Many sclerotic plaques were about the coronary openings. The right coronary vessels were not patent. The left coronary vessels were free but sclerosed. The aortic ring was much dilated, 10.5 cm. in circumference. The whole intima of the aorta was very much thickened. Here and there were areas of sclerosis. The openings of the large vessels were dilated. Eight centimeters beyond this there was an opening on the left posterior wall of the aorta 2 cm. in diameter, opening into a sac 4 cm. in diameter. The body of the fifth thoracic vertebra had been slightly eroded. Beyond this the thoracic aorta was much thickened in irregular areas. About 1,000 c.c. of straw-colored fluid was in the left pleural cavity. The abdomen contained about 10 liters of cloudy fluid with many shreds of fibrin. The visceral and the parietal peritoneum was dark in color and covered with exudate. The intestines were adherent. The liver showed no scarring; weight 1,660 grams. In the kidneys the cortex was not sharply differentiated from the medulla. The whole kidney was dark in appearance, with cloudy swelling to parenchymatous change. For these details I am obliged to Dr. A. A. Johnson.

III. MISCELLANEOUS VASCULAR CONDITIONS INCLUDING VASCULAR NEUROSES

Among these are three cases of Raynaud's disease.

Margaret H., aged 15, suffering from Raynaud's disease in the fingers, had a flow in the right hand of 5.33 grams per 100 c.c. of hand per minute and 6.67 grams in the left, with room temperature 23.6 C. The protocol has already been published.[6] The considerable inequality in the flow in the two hands is probably due to a functional vasomotor difference. When there are no anatomical reasons for such a difference in flow it either disappears at subsequent examinations or is reversed as regards the two hands. In cases in which a marked difference is obtained in the two hands in several examinations, the deficiency being always in the same hand and the ratio of the flows in the two hands not changing greatly, there is reason to believe, in the absence of obvious anatomical differences, that the difference in flow may depend on pathological changes in the thorax or in the arm or hand itself which have not yet definitely disclosed themselves by other symptoms.

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[6] Heart, 1911, iii, 79.

The flow in Margaret H. is distinctly subnormal, which corresponds with the fact that her hands were cold to the touch, although she did not have an attack during the examination. The relatively small flow may be related to the tendency to dyspnea which she states has existed for some years. The most striking result of the examination was the intense reflex vasoconstriction produced in the left hand when the right was put into cold water, the flow being reduced from 6.67 grams to 2.97 grams per 100 c.c. per minute. Although intense, the vasoconstriction was transient, lasting only for two minutes and then giving place to distinct vasodilatation, the flow increasing to 8.28 grams in the left hand, while the right continued in the cold water. Immersion of the right hand in warm water produced no further increase, but rather a decrease. The vasomotor mechanism of the hand seems, therefore, to respond with abnormal readiness to vasoconstrictor influences and with less than normal readiness to vasodilator influences. The short duration of the intense crossed reflex vasoconstriction relates the case to those of early peripheral neuritis,[7] and it is of interest, in this connection, that neuritic changes may be associated with the Raynaud's syndrome.

The second case of Raynaud's disease was that of Mrs. W. G., aged 28, who was seen April 24, 1911. About one and one-half years previously, after a sleigh ride, she noticed that the fingers of both hands became cold, "white like those of a dead person" and numb. Sometimes the fingers became purple. All the phalanges were involved. She feels sure they were not frost-bitten. Since that time she has had many attacks, each lasting usually five to ten minutes, but occasionally almost an hour. The attack generally begins in the thumb. Putting the hands into cold water does not necessarily bring on an attack. A cold full bath is more likely to do so. The thumbs are apt to become numb if she holds anything in her hands for any length of time. Long before this condition came on her arms and hands used to go to sleep a great deal even when she was not lying on them. Also for as long as she can remember small injuries to the skin of the hands or arms healed badly. She pointed out the scar of a small burn on the left hand which was still raised above the surface although otherwise healed. It was a most trifling burn she said. Even a little scratch leaves a scar. She showed various marks of old injuries on the arm. She has been fighting the condition by going out to walk without gloves, continuing to walk with her hands exposed even when they became numb, and thought that some time she improved it in this way, her hands afterwards becoming warm. Her general method has been to immerse them in warm water on coming in. The attacks are apt to be induced by a damp day, even if not cold. The hands to-day feel markedly cold to the touch, not only the fingers, but the hands midway to the wrists. The day was not cold and she was wearing kid gloves. Her arms are mottled with purple spots. She has no trouble in the feet, nose, or elsewhere. Her general health is satisfactory, but there is some shortness of breath on exertion. She is fat and well nourished, and the arms and hands are quite plump. She suffers much from nervousness.

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[7] Paper XII of this series.

The blood-flow in the hands was examined April 24, 1911. Pulse 108 (sitting). Mouth temperature 37.55 C. Hands put into bath at 10:10 a. m. At 10:15 it was seen that the left arm was getting purple; the right arm remained unchanged. She said the left hand felt colder than the right, and that the left arm and hand felt as if swollen. Hands put into calorimeters at 10:20 a. m.

TABLE 11.—Calorimetric Measurements in Case of Mrs. W. G.

Time	Right	Left	Notes
10:19	30.125	30.13	
10:24	30.11	30.13	
10:25	30.12	30.15	Room temp. 25.3 C.
10:27	30.17	30.19	
10:28	30.20	30.22	
10:29	30.22	30.24	
10:30	30.25	30.26	
10:31	30.26	30.26	
10:32	30.27	30.27	
10:33	30.29	30.31	
10:34	30.31	30.32	At 10.34 put left hand in water at 43 C.
10:35	30.33	.....	
10:36	30.36	.....	Room temp. 27 C. Face and ears red. She says the left hand feels swollen greatly.
10:37	30.38	.....	
10:38	30.40	.....	
10:39	30.42	.....	Room Temp. 25.3 C.
10:40	30.47	.....	
10:41	30.50	.....	
10:42	30.54	.....	
10:43	30.57		
10:44	30.60		
10:45	30.62		
10:46	30.67		Room temp. 24.9 C.
10:47	30.70		At 10:47 left hand put in water at 12 C.
10:48	30.71		
10:49	30.72		
10:50	30.73		
10:51	30.75		
10:52	30.77		
10:53	30.79		
10:54	30.81		At 10:54 dried and wrapped left hand. It is red and is not specially cold to touch. Room temp. 27.4 C.
10:55	30.83		
10:56	30.86		
10:57	30.89		
10:58	30.92		Hand out of calorimeter at 10:58.
10:59	.....		10:59 temp. of L. is 30.30 C.
11:24	30.74		11:24 temp. of L. is 30.06 C. Room temp. 25.8 C.

Cooling of calorimeters, R., 0.18 C. degree in twenty-six minutes; L., 0.14 degree in twenty-five minutes. Volume of right hand 391 c.c., of left hand 375 c.c. Water equivalent of calorimeters with contents, R., 3,408; L., 3,395. The left hand may be swollen a little, as her ring, which had been removed, now goes on with difficulty, yet the subjective feeling of extreme swelling which she had is obviously no index of the actual swelling.

The small initial flow in this patient (3.62 grams per 100 c.c. per minute for the right hand and 3.44 grams for the left, with the relatively high room temperature of 25.3 C.) is considerably more striking than in the case of Margaret H. This agrees well with the longer duration and greater development of the condition in Mrs. W. G. Immersion of the left hand in warm water caused a fair and persistent increase in the flow in the right (to 5.16 grams), although the absolute flow was still small. Subsequent immersion of the left hand in cold water caused a strong vasoconstriction in the right hand, diminution of the flow to 2.46 grams per 100 c.c. per minute for the first three minutes and 3.93 grams for the last four minutes. Although the temperature of the cold water was purposely made higher than usual (12 C. instead of 8 C.), she complained greatly of the cold and withdrew her hand intermittently. This was seen also in the other cases, and the hypersensitiveness of the afferent receptors to cold as gauged by the sensation elicited has its parallel in their hypersensitiveness to cold as components of the reflex vasomotor arc.

The third case of Raynaud's disease (Mrs. C. B.) illustrates the condition when it has existed for a long time and has gone on to gangrene. The age of the patient was 29. Not only was the local condition more severe than in the last case, but the general physical condition was worse. The hand flow for a period of sixteen minutes before the vasomotor reaction was tested was 3.23 grams per 100 c.c. per minute for the right hand and 4.29 grams for the left. For the last six minutes of this period the flows worked out at 3.65 grams and 3.80 grams for the right and left hands, respectively. The reflex reaction to warmth was fair (the flow in the right hand increasing for the first two minutes of immersion of the left in warm water to 6.55 grams per 100 c.c. per minute), but it was transient, and for the last ten minutes of the period the flow was only 4.30 grams per 100 c.c. per minute. The reflex reaction to cold was also anomalous, possibly because of the existence at this stage of the disease of considerable anatomical changes in the vessel.

Mrs. C. B., aged 24, was admitted to the Lakeside Dispensary June 1, 1908, suffering from Raynaud's disease. She was treated with nitroglycerin without benefit. April 23, 1913, on account of coughs, sweats, and general weakness she was referred to the Medical Department of the Dispensary when the following data were elicited. Both hands are affected. The condition was first noted one day in winter seven years ago, the fingers becoming cold and pale and then getting purple. The attacks have been growing steadily worse, especially in the last five years. Sometimes small grangrenous areas form quickly at the ends of the fingers and quickly recover, but always with some loss of substance, so that the terminal phalanges of several of the fingers have lost a considerable proportion of their length and most of them have lost their nails. On all the fingers the nails are atrophic. She has considerable pain in the fingers when they "break out." She has had pain and marked stiffness in the right wrist and right forearm for about two years, and she uses the right hand but little on account of the stiffness of the wrist. The skin of the right forearm is somewhat stretched and distinctly glossy in comparison with that of the left. She cannot bear to put her hands into cold water. She has no such symptoms in her feet, nose or elsewhere. Some years ago she had a sore on her ankle, due, as she thinks, to a habit of kicking the ankle with the other foot. The sore refused to heal and she was put in hospital for several weeks, during which time her general health and strength improved greatly, and the sore also improved, although it took a long time before it was healed. She is pale and thin. There is some pigmentation of the skin and some dulness at the apex of the left lung. The radial pulse is small.

Examination of the blood-flow in the hands was made May 9, 1913. The marked pallor with some lividity and the "stone cold" feeling of the hands, especially of the fingers, was striking, although she was wearing gloves. The day was rather chilly. The terminal phalanx of one finger of the right hand had a small sore on the point of it which she said caused her some pain. Pulse (sitting) 112, weak. Hands in bath at 3:15 p. m., in calorimeters at 3:27. Mouth temperature, 37.35 C.

TABLE 12.—CALORIMETRIC MEASUREMENTS IN CASE OF MRS. C. B.

Time	Right	Left	Room Temp. C.	Time	Right	Notes
3:26	31.18	31.17	.....	3:53	31.135	3:52 left hand put in water at 43 C.
3:28	31.09	31.13	.....	3:54	31.155	Room 22.8.
3:29	31.09	31.13	21.3	3:55	31.16	
3:30	31.08	31.12	.....	3:56	31.17	Room temp. 22.9 C.
3:31	31.08	31.12	21.5	3:57	31.175	
3:32	31.08	31.11	.....	3:58	31.18	
3:33	31.085	31.11	.....	3:59	31.195	Room temp. 22.95 C.
3:34	31.08	31.11	21.8	4:00	31.20	
3:35	31.08	31.11	.....	4:01	31.20	
3:36	31.08	31.115	.....	4:02	31.205	
3:37	31.085	31.12	22.0	4:03	31.21	
3:38	31.085	31.12	.....	4:04	31.225	At 4:04 left hand put in water at 12 C.
3:39	31.085	31.125	.....	4:05	31.24	She feels it very cold. Left hand taken out of water intermittently.
3:40	31.09	31.14	.....	4:06	31.25	
3:41	31.085	31.15	22.1	4:07	31.255	Room temp. 22.7 C.
3:42	31.09	31.16	.....	4:08	31.26	The cold water is now at 13.5 C. The left hand is red. She says if it had not first been in warm water it would have been purple in the cold water. To the touch the left wrist is warm (vasodilatation), much warmer than the right.
3:43	31.09	31.17	.....	4:09	31.27	
3:44	31.09	31.18	.....	4:10	31.28	
3:45	31.09	31.195	.....	4:11	31.295	
3:46	31.095	31.20	22.0	4:12	31.305	
3:47	31.10	31.205	.....	4:13	31.34	4:13 hand out calorimeter.
3:48	31.10	31.21	.....	4:43	30.96	4:43 temp. L. 30.58 C.
3:49	31.105	31.215	.....			
3:50	31.115	31.22	22.6			
3:51	31.12	31.225	.....			
3:52	31.12	31.23	.....			

Cooling of calorimeters, R., 0.38 C. in 30 minutes; L., 0.65 C. in 51 minutes. Volume of right hand 273 c.c., of left 282 c.c. She is right handed. Water equivalent of calorimeters with contents, R., 3.313; L., 3.320.

It may be noted that in these three cases of Raynaud's disease there was evidence that a coexisting or preexisting general feebleness of the circulation conspired with the local condition in producing the symptoms. The blood-flow measurements suggested that if the general circulatory conditions had been normal the local tendency to vasoconstriction might not have sufficed to reduce the flow to the level at which the symptoms became obtrusive. This was the suggestion merely derived from the three cases studied and it is not claimed that it has a general application. At any rate since hand flows habitually as small or smaller are often encountered in cases which never develop Raynaud's disease. the primary factor must be a tendency, whatever its essential cause, to the local diminution in the flow.

In a case of "dead fingers" in an elderly man affecting only the right hand, the flows were among the smallest observed in the whole investigation, and this not only in the hand obviously affected, but also in the other. The patient had been sitting in a well-warmed room for an hour before the examination, yet the calculated flow for the right hand was only 0.09 gram per 100 c.c. per minute and for the left 0.25 gram, with room temperature 20.5 C. A fair reflex vasodilatation was obtained in the right hand on the immersion of the left in warm water, the flow increasing to 0.5 gram, still of course a very small flow, but relatively a great increase. The dead condition of the right hand is therefore probably not due to anatomical change in the vessels, but to a vasoconstriction.

The next case in this group is that of Maurice T., a man 41 years old, who had lost a leg through obliterative arteritis.

Maurice T., a tailor's cutter, height 5 feet 7 inches, weight about 175 pounds, a well-built man, apparently in perfect health. He was seen April 17, 1911. About eight years ago in winter he began to feel the toes of the left foot cold. The little toe was first affected; gradually the same condition came on in the other toes. After awhile the toes became painful also. The whole foot became involved by degrees. Then cramp-like pains began to trouble him in the calf of the left leg. The trouble was worse in winter. Small nodules on the foot and toes became gangrenous. Eventually, four years ago, the left leg had to be amputated above the knee. The arteries were found extensively affected. He never had any pain above the knee. About six months ago he noticed that the little toe of his right foot was cold. Later on it began to pain him. Now the whole right foot is cold to the touch and the pulse in the dorsalis pedis poor. The little toe has a raw surface where it is contact with the next toe and the nail is apparently going to come off. He knows of no injury to it. The pain in the foot is so great that while he is in bed he cannot sleep. When he stands the pain disappears, but he has pain also when he walks. The arch of the right foot is broken down and he has to wear a support in his shoe. There is hyperidrosis of the foot in spite of the fact that it is cold. The flow in the hands was examined April 17, 1911. Mouth temperature 36.5 C. Hands put into bath at 10:05 a. m. and into calorimeters at 10:18. Pulse (sitting), 92.

At this time the foot calorimeters had not been constructed so that only an examination of the flow in the hands was made. This was done with the idea that some information of possible value for a prognosis in regard to the leg condition might be obtained, (1) from the absolute amount of the hand flow as an index of the flow in the periphery in general, (2) from the nature of the reflex vasomotor response as an index of the existence of a tendency to vasomotor spasm, a functional condition which there is good reason to believe may underlie or at least precede in certain cases the development of obliterative arteritis. The flow in the right hand was 4.87 grams per 100 c.c. per minute and in the left 6.67 grams, with room temperature 25.7 C., a distinctly subnormal flow. Immersion of the right hand in cold water caused one of the most intense reflex vasoconstrictions in the contra-lateral hand which has been witnessed in the whole course of these observations, the flow declining to 2.59 grams per 100 c.c. per minute for the first five minutes and only reaching 5.59 grams after a further immersion in the cold water of four minutes. The reflex to warmth is also well marked, the flow in the left hand eventually rising to 10.96 grams. The general indication of the observations as regards the question propounded was that a vasomotor instability with a tendency to excessive vasoconstriction in the extremities might be the basis for the symptoms in the foot. The inequality in the flows in the two hands corroborates the idea of some degree of vasomotor abnormality. Anatomical changes in the nerves were of course not excluded. Unfortunately, the man soon after removed to a distant part

TABLE 13.—Calorimetric Measurements in Case of Maurice T.

Time.	Right	Left	Notes.
10:17½	29.57	29.58	
10:20	29.58	29.60	
10:21	29.60	29.62	
10:22	29.62	29.65	Room temperaature 25.7 C.
10:23	29.66	29.70	
10:24	29.70	29.76	
10:25	29.74	29.82	
10:26	29.78	29.86	Room temperature 25.6 C.
10:27	29.81	29.92	
10:28	29.85	29.97	Room temperaature, 26 C. Ears red.
10:29	29.89	30.02	
10:29½	....	....	Right hand put in water at 9 C.
10:30	....	30.08	
10:31	....	30.09	
10:32	....	30.11	The cold water is now 10.6 C.
10:33	....	30.12	He feels the cold water extremely.
10:34	....	30.14	Room temperature 26. 6 C.
10:35	....	30.15	
10:36	....	30.19	
10:37	....	30.22	
10:38		30.24	Room temperaature 25.5 C.
10:39		30.29	At 10:39 put right hand in water at 43°.
10:40		30.31	
10:41		30.34	Room temperature 25.0 C.
10:42		30.38	Room temperature 25.1 C.
10:43		30.45	
10:44		30.52	Room temperature 25.2 C.
10:45		30.60	Ears still red.
10:46		30.65	
10:47		30.72	Room temperature 25.2 C.
10:48		30.80	At 10:48 dried and wrapped right hand.
10:49		30.82	
10:50		30.88	Room temperature 25.2 C.
10:51		30.94	
10:52		31.00	Room temperature 25.3. C.
10:53		31.07	
10:54		31.13	Hand out of cal.
11:09		....	Temp. of room 29.65 C.
11:09½		31.01	

Volume of right hand, 470 c.c.; of left hand, 466 c.c. He is right-handed.

of the country, and up to the present it has not proved possible to learn the further history of the case.

In the case of Anthony P., a man 36 years old, with gangrene of the fingers and toes, the question arose whether the condition depended on a vasomotor neurosis.

Anthony P., a Polish laborer, aged 36 years, height 5 feet 8 inches, weight 150 pounds, was admitted to City Hospital, Oct. 9, 1912, complaining of sore fingers and toes. He froze his feet last winter. There is no history of frost-bite of the fingers. He had numbness of the fingers a year ago. Owing to the condition of his fingers he was forced to quit work about three weeks before admission. On admission the right hand showed beginning gangrene at the tip of the thumb, loss of the distal half of the nail of the middle finger, the remainder being undermined and loss of the entire nail of the ring-finger. The left hand showed purplish discoloration of the thumb, the nail being absent, loss of the entire nail of the index finger except the root, and gangrene about the base of the nail of the ring-finger.

A blood-flow examination of the hands was made on Oct. 11, 1912, with a very warm day (room temperature 27.8 C.). The flow came out only 1.22 grams for the right hand, and 1.12 grams for the left per 100 c.c. per minute, or allowing for the swelling of the left hand, 1.27 grams. The pulse-rate was 120 (sitting). The conclusion drawn was that if the small flow depended solely on the local conditions it was unlikely that the constriction of the vessels was purely functional, since the high room temperature would have caused vasodilatation. He was in such poor condition that a sufficient examination of the vasomotor reflexes was postponed. In the meantime cyanosis of the face and dilatation of the neck veins became prominent and physical examination revealed the signs of serious involvement of the heart (mitral stenosis, aortic insufficiency and signs of impairment of the myocardium). It was no longer possible to draw deductions from the small hand flow, and the slight response to the high external temperature as to the condition of the local circulation, since the state of the heart itself was sufficient to account for the small flow even provided that the cutaneous vasodilatation was the maximum possible with so small a driving power. Also fever (his rectal temperature was 39.65 C.) is associated with cutaneous vasoconstriction and a small hand and foot flow.[8] Had the feet been normal, a comparison of the hand and foot flow might still have yielded information, since the cardiac insufficiency might be expected to diminish the flow in both without affecting the normal ratio between the hand and foot flow, whereas a vascular constriction (vasomotor or anatomical) confined to the hands would be revealed by a disturbance of this ratio in favor of the feet. The local conditions, however, soon became a matter of indifference in view of the serious involvement of the heart. The patient died October 12.

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[8] Stewart, G. N.: Paper VIII, Jour. Exper. Med., 1913, xviii, 372.

The necropsy showed the following: Left lung: infarct in the lower lobe 5 cm. in diameter. Right lung: infarct in upper lobe 2½ cm. in diameter, and in lower lobe 5 cm. in diameter. Heart engorged on the right side and left side dilated; heart-muscle dark and flabby. The pericardium contains 100 c.c. of fluid. Aortic valve, left cusp hardened and shortened. Mitral admits tip of index-finger. Vegetations about the valves. Tricuspid, edges of valves thickened, recent vegetations. Liver, 1,800 grams, with chronic passive congestion. Spleen, weight 140 grams, chronic passive congestion. The kidneys show much arterial thickening. Blood-vessels: radial, practically no arterial thickening. The fingers show stasis of blood in the vessels. A cross-section of the index-finger shows much perivascular infiltration, but no thickening of the vessel walls. Pathological diagnosis, septic endocarditis.—(From Dr. Johnson's report.)

In a case of diabetic gangrene of the feet in a man 63 years old, the flow with a room temperature of 25.6 C. was 1.39 grams for the right foot and 1.83 grams for the left, or allowing for the swelling of the latter 1.95 grams. An interesting point is that the flow in the foot in which the gangrene had made most progress was greater than in the other foot. There is scarcely any question that this is due to inflammatory reaction. The diminished flow in the toes actually involved, if the flow is diminished there, would not show in a measurement of the flow through the whole foot. The sum of the flows in the feet, although subnormal, is not strikingly deficient, and the ratio of foot to hand flow (1:1.85) falls within the normal range. The hand flow was measured on the day preceding the observations on the foot and came out 2.65 grams for the right hand and 3.32 grams for the left per 100 c.c. per minute, with room temperature 22.0 C. In hospital cases presenting no rapid clinical changes, our experience has shown that such observations can safely be compared. The fact that the flow both in the hands and feet is decidedly below the normal agrees with the well-known feebleness of the cutaneous circulation in diabetes, and is probably in part due to cardiac changes. The vasomotor reflex, when warm water is applied to the contralateral hand, is very poor. Whether this indicates the beginning of pathological changes in the hand arteries also cannot of course be definitely stated. It is in any case interesting to correlate the enfeeblement of this vasomotor reflex with the enfeeblement or disappearance of skeletal reflexes such as the knee-jerk, which is known to occur in long-standing cases.

James P., a teamster 63 years old, was admitted to the City Hospital, Aug. 16, 1911, with a small ulcer on the inner surface of the left great toe and a scar in the same position on the right great toe. He came for treatment for his foot. It was found that the urine contained 4 per cent. of sugar with a trace of albumin. He was put on a diabetic diet. The blood-count showed erythrocytes 4,890,000, leukocytes 7,800, hemoglobin 90 per cent. April 28, 1912, the percentage of sugar in the urine was reduced to 0.8. April 11, 1912, when the blood-flow in the feet was examined there were small necrotic areas on the great and second toes of the right foot. The distal half of the left foot was bluish-red and the foot considerably swollen. The toes of the right foot were also bluish-red. He says that sometimes the left foot is hot, but when the flow in the feet was examined this was not the case.

Feet in bath at 1:21 p. m.; in calorimeters at 1:33, and out of calorimeters at 2:00; 3,740 c.c. of water in each calorimeter.[9]

Mouth temperature 37.45 C. Pulse (sitting), 68.

TABLE 14.—CALORIMETRIC MEASUREMENTS IN CASE OF JAMES P.

Time.	Right	Left	Room Temp. C.	Time.	Right	Left	Room Temp. C.
1:37	30.82	30.76	....	1:51	30.995	30.97	....
1:38	30.82	30.80	25.9	1:52	30.98	31.00	....
1:39	30.86	30.82	....	1:53	31.01	31.01	25.4
1:40	30.875	30.83	....	1:54	31.02	31.025	....
1:41	30.885	30.84	....	1:55	31.03	31.04	....
1:42	30.885	30.855	25.8	1:56	31.035	31.05	....
1:43	30.905	30.87	....	1:57	31.05	31.06	....
1:44	30.92	30.88	....	1:58	31.05	31.08	....
1:45	30.935	30.915	....	1:59	31.06	31.10	....
1:46	30.94	30.92	....	2:00	31.02	31.09	25.4
1:47	30.95	30.935	....	2:28	30.76	.....	....
1:48	30.96	30.95	25.2	2:29	.....	30.75	....
1:49	30.975	30.96	....	2:32	30.71*	.....	....
1:50	30.98	30.96	....	2:33	......	30.72*	....

* After better stirring.

Cooling of calorimeters, R., 0.31 degree in thirty-two minutes, L., 0.37 degree in thirty-three minutes. Volume of right foot in calorimeter 1,090 c.c. of left foot 1,175 c.c. Rectal temperature (taken by himself and doubtless too low as compared with mouth temperature), 37.5 C. Water equivalent of calorimeters with contents, R., 4,760, L., 4,820.

The next case is remarkable for the fact that the flow in the hands per 100 c.c. per minute was very much less than in the feet, a quite unusual circumstance.

K., a laborer aged 50, was admitted April 15, 1912, to the City Hospital. He was much cyanosed on admission, and when the flow in the hands was first examined next day the cyanosis was still well marked in the face, nose, ears and hands, although less pronounced than on admission. There is gangrene of the toes on left foot. The pulse can be felt in the dorsalis pedis. Blood-pressure 140 systolic, 100 diastolic. He had some cough and râles of every description were heard all over the lungs. The fingers were markedly clubbed. The heart-sounds were weak. A soft systolic murmur and reduplicated second sound were heard over the left sternal border, more marked at the base. The heart was enlarged. The pulse at the wrist is not strong, but by no means so weak as to suggest that the blood-flow in the hands would be found so small as is actually the case.

April 16 the flow in the right hand came out only 0.27 gram per 100 c.c. per minute and in the left hand 0.28 gram, for a period of eighteen minutes in the calorimeters, with room temperature 23.8 C. Immersion of the left hand in warm water caused no increase whatever in the flow in the right. The very small flow in the hands agreed with the diagnosis of myocarditis. It is possible also that a factor in the small flow was nervousness, as this was the first examination, and the patient was a foreigner, speaking no English. Still the effect of nervousness on the flow usually passes away more quickly.

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[9] For the details of measurements of foot-flow see Paper VII of this series, Jour. Exper. Med., 1913, xviii, 354.

April 18 he was again examined. The cyanosis was now much diminished and the radial pulse was stronger. The flow in the right hand was 1.05 grams and in the left 1.43 grams per 100 c.c. per minute, with room temperature 22.5 C., still quite a small flow, although much greater than at the last examination. In the right foot the flow was 2.15 grams per 100 c.c. per minute, and in the left foot 3.42 grams. Immersion of the right foot in cold water was accompanied by a reduction in the flow in the left foot to 2.68 grams, which was only slightly increased (to 2.87 grams) when the right foot was put into warm water.

Feet in bath at 2:07 p. m., in calorimeters 2:19 p. m. Patient sitting. 3.740 c.c. water in each calorimeter. At 2:45 p. m. the right foot was put into water at 10.5 C.

TABLE 15.—CALORIMETRIC MEASUREMENTS IN CASE OF K.

Time	Right	Left	Room Temp. C.	Time	Left	Notes
2:22	29.99	29.93	.....	2:46	30.605	
2:23	30.00	29.95	20.5	2:47	30.625	
2:24	30.02	29.99	.....	2:48	30.635	Room temp. 20.7 C.
2:25	30.03	30.05	.....	2:49	30.655	
2:26	30.045	30.08	.....	2:50	30.665	
2:27	30.07	30.125	.....	2:51	30.70	
2:28	30.08	30.14	20.4	2:52	30.715	
2:29	30.09	30.175	.....	2:53	30.725	
2:30	30.10	30.22	.....	2:54	30.745	At 2:54 right foot put in water at 42.8 C.
2:31	30.11	30.245	.....			
2:32	30.125	30.275	.....	2:55	30.76	Room temp., 21.0 C.
2:33	30.135	30.30	.....	2:56	30.775	Right big toe painful.
2:34	30.145	30.33	.....	2:57	30.80	
2:35	30.17	30.35	20.1	2:58	30.825	
2:36	30.19	30.38	.....	2:59	30.835	
2:38	30.21	30.42	.....	3:00	30.85	
2:39	30.22	30.46	.....	3:01	30.87	
2:40	30.23	30.47	.....	3:02	30.90	Room temp.· 21.3 C.
2:41	30.23	30.50	.....	3:03	30.925	
2:42	30.235	30.52	.....	3:04	30.935	
2:43	30.24	30.535	.....	3:05	30.94	Foot out of calorimeter.
2:44	30.26	30.56	.....	3:17	30.75	Room temp. 20.9 C.
2:45	30.275	30.595	.....	3:18	.....	Temp. of R. is now 29.79 C.

Cooling of calorimeters, R., 0.485 C. in thirty-three minutes; L., 0.19 C. in twelve minutes. Rectal temperature 37.6 C. Volume of right foot in calorimeter 950 c.c., of left 985 c.c. Water equivalent of calorimeters with contents, R., 4,652; L., 4,679.

The question whether the gangrene was going to spread was what chiefly interested the physician in charge of the case. The fact that the flow in the feet was so good was interpreted as favorable for the prognosis, although of course it was impossible to say to what extent the flow in the toes themselves had been interfered with. The left foot was somewhat swollen, as shown by the volume measurement. Yet it was only a little over 3 per cent. larger than the right. The greater flow in the left was probably related to a certain degree of inflammatory reaction. The foot soon began to heal up. But on April 25 the temperature, which had hitherto never surpassed 100 F., began to rise, reaching 104.2 F. on April 27. Then it fell and remained below 100 F. till his death on May 3.

The existence of a relatively good flow in the feet associated with a poor flow in the hands demands some further remark. It is probable that the immediate cause of the lesion in the left foot was exposure to cold. If so, it is likely that the already existing feebleness of the circulation and the poor response of the vasomotor regulatory mechanism were contributing causes. Very likely both feet suffered injury, although it only went on to gangrene in the left. The flow in both feet may, therefore, have been increased by the reaction to the injury caused by the freezing, and this in spite of the feeble driving-power of the heart. Thus the flow in the feet may have been brought up by the accident of the inflammation approximately to the normal flow, while that in the hands fell far below the normal.

Miss W., aged 25, weight 128 pounds, has lost fourteen pounds since her illness began. She first noticed pain in the ankles with some swelling in March, 1908. The pain increases as the day goes on, and at about 7 p. m. it is worse but on lying down she gets relief. In the morning her eyes are swollen. The wrists also swell when she works much with her arms. There is some shortness of breath. She must lie down some part of the day if she desires to sit up at night, even to 9 o'clock. An eruption consisting of raised red spots comes out periodically on the legs, also, though much less copiously, on the arms. There is burning pain and itching in the spots. In a day they get brownish, and in two days have disappeared to a great extent, except that a brown stain persists for weeks. Several spots 2 cm. in diameter which had come out the previous day on her legs were examined. The reddish color did not diminish on pressure. From her description the spots resemble urticaria at first and then hemorrhage takes place into the wheals. On the trunk also are spots which she describes as wheals, which itch and are painful, but the most purpuric-looking spots are on the legs. On the front of each tibia is a spot with a blackish crust from which she says some matter came out, but generally no liquid escapes from them. Her feet and toes are cold and so are her hands, especially the terminal phalanges of the fingers. Her nails grow irregularly, probably more quickly than before, and are ridged. There is distinct defect of sensation in the toes and the adjacent parts of the foot. A pin-prick is scarcely felt, and then only as contact. She does not feel any tickling sensation when the sole is stroked and there is no plantar reflex. Good knee-jerks can be obtained. There is a long reddish scar on the back of one finger of the left hand. She says she had "blood-poisoning" some time ago in a small wound caused by a tack and healing did not occur for eighteen weeks. The heart-sounds are clear and unaccompanied by murmurs. The urine contains no albumin, casts or sugar. Her eye-sight is not affected.

The blood-flow in the hands was examined May 9, 1911. Pulse 88. Mouth temperature 37.6 C. Hands put into bath at 10:14½ p. m., and into calorimeters at 10:24.

TABLE 16.—CALORIMETRIC MEASUREMENTS IN CASE OF MISS W.

Time.	Right	Left	Notes.	Time.	Right	Notes.
10:23	30.13	30.08	Room tempera- 24.0 C.	10:43	30.195	Room temperature 24.3 C.
10:25	30.11	30.06		10:44	30.20	
10:26	30.10	30.05		10:45	30.215	At 10:45 left hand put in water at 9.1 C. She feels left hand very uncomfortable.
10:27	30.11	30.05		10:46	30.215	
10:28	30.09	30.04		10:47	30.22	
10:29	30.10	30.04	Room tempera- 24.1 C.	10:48	30.225	Room tempera- 24.3 C.
10:30	30.10	30.04		10:49	30.225	
10:31	30.10	30.03		10:50	30.23	
10:32	30.12	30.04		10:51	30.23	
10:33	30.12	30.035		10:52	30.235	Room temperature 24.4 C. At 10:52 dried and wrapped left hand. It is pretty red.
10:34	30.125	30.04		10:53	30.235	
10:35	30.13	30.045		10:54	30.24	
10:36	30.145	30.06		10:55	30.245	Room temperaature 24.5 C.
10:37	30.16	30.06	At 10:37 left hand put in water at 43 C.	10:56	30.245	Hand out of calorimeter. Feels pins needles in it.
10:38	30.165	......	Room temperature 24.3 C.	10:56½	......	Temperature of L., 29.91 (at 10:56½).
10:39	30.17	......	Left hand is fairly red and the veins of fair size.	11:26	30.03	
10:40	30.17	......				
10:41	30.18	......				
10:42	30.185	......				

Cooling of calorimeters, R., 0.215 C. in thirty minutes, L., 0.15 C. in nineteen and one-half minutes. Volume of right hand in calorimeter 292 c.c. of left 298 c.c. She is right-handed.

May 25, 1911, the physician in charge of the case reported that since the time of the blood-flow examination she had had rather severe intestinal symptoms and that her temperature rose to 103 F. He gave her calcium chlorid and alkalies. She is now much better than for a while and the spots have disappeared.

The flow in the right hand was 2.16 grams per 100 c.c. per minute, in the left 1.64 grams, with room temperature 24.1 C., a very poor flow for her age. Reflex vasodilatation is absent, or quite feeble, the flow in the right hand only rising to 2.38 grams when the left was immersed in warm water. Scraping the skin with a blunt point caused no local vasodilatation. Although the initial flow was so small a further reflex vasoconstriction, reducing the flow in the right hand to 1.72 grams, was obtained when the left hand was put into cold water. No doubt the coexisting anemia is a factor in reducing the flow through the hands. The toxemia (rheumatic perhaps) on which the purpura depends may also depress the flow more directly, either by enfeebling the heart or by vasoconstriction. The conclusion deduced from the blood-flow measurements was that the feeble cutaneous flow might be a factor in the condition, and that so far as this went, the indication was that such measures should be adopted as would increase the flow in the skin, including the treatment of such anemia as was present.[10]

The last case to be described in this paper is that of Charles H.

Charles H., a clerk 42 years old, height 5 feet 10½ inches, weight 140 pounds, was admitted to the City Hospital Nov. 23, 1912, with edema of the right foot and leg. The swelling began a month ago, commencing at the toes with inflammation, he says, resembling erysipelas. A little over a year ago he accidentally injured the right lower leg by a blow with a hammer about midway between knee and ankle over the tibia. It healed at the time. Afterward a sore opened from which matter was discharged. He entered a hospital, where the leg soon healed. He has pain as soon as he commences to walk. When he stands up for a few minutes the foot becomes very blue and the small blood-vessels distend. The swelling comes on with great rapidity (in ten or fifteen minutes) when he goes about on his feet, and disappears completely when he lies down for a little while. There are no varicose veins. He does not appreciate warmth or cold, or contact (blunt-point) on the dorsum of the right foot or on the lower third of the right leg. A pin-prick is felt as dull contact. There is no anesthesia above the level of the scar due to the injury, except for a small tongue just above and continuous with the scar. The right sole is very sensitive. It began to be hypersensitive just after the foot commenced to swell. When he awakes in the morning he has a burning sensation about the toe-nails of the right foot. This disappears when he walks about a little. When he stood up it was seen that his right leg became very red in the anesthetic region. On pressure the red color disappeared. He says that when he first came into the hospital the white spot produced on pressure remained for some time, but now it quickly becomes red again. When he first came into the hospital

TABLE 17.—Calorimetric Measurements in Case of Charles H. First Examination

Time	Right	Left	Room Temp. C.	Time	Right	Left	Room Temp. C.
3:26	31.43	31.43	....	3:51	31.15	31.165	....
3:29	31.36	31.31	22.7	3:53	31.135	31.18	23.0
3:31	31.33	31.26	....	3:55	31.125	31.185	23.1
3:33	31.305	31.24	22.8	3:57	31.12	31.19	23.15
3:35	31.28	31.23	23.1	3:59	31.105	31.21	23.1
3:37	31.26	31.195	23.15	4:01	31.09	31.225	....
3:39	31.235	31.18	....	4:03	31.08	31.24	23.0
3:41	31.22	31.17	23.1	4:05	31.07	31.24	....
3:43	31.20	31.16	....	4:07	31.06	31.245	23.0
3:45	31.18	31.155	23.1	4:10	31.01	31.18	....
3:47	31.17	31.155	23.0	4:21	30.865	31.04	....
3:49	31.16	31.15	....	....	.....	.....	....

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[10] Paper VI of this series, Jour. Exper. Med., 1913, xviii, 13.

the red color which came on when standing soon became pale blue, whereas after a fortnight in the hospital it remains red. The legs, however, continue to be cold to the touch. He would not know his leg and foot were becoming red if he did not see it. He says he cannot keep the right foot warm. When the left foot is sweating under the bedclothes and he puts his hand down to feel the right foot it is always cold. He looks anemic and feels pretty weak, though his appetite is good. He has lost nearly 30 pounds in weight since he had malaria in Texas three years ago. The knee-jerks and ankle-jerks are somewhat exaggerated, but there is no patellar or ankle clonus. Examination of the heart and lungs is negative in result and the heart sounds are clear though very weak and distant. The pulse is regular.

The flow in the feet was examined Dec. 5, 1912, the patient sitting. Feet in bath at 3:15 p. m., in calorimeters at 3:28, and out of calorimeters at 4:07; 2,775 c.c. of water in each calorimeter. (Table 17.)

Cooling of calorimeters in eleven minutes, R., 0.145 degree; L., 0.14 degree. Volume of right foot 961 c.c., of left 924 c.c. He has small feet (No. 7 shoes). Rectal temperature 37.6 C. Pulse (sitting) 100. Water equivalent of calorimeters with contents, R., 3,696, L., 3,668.

Second examination Dec. 10, 1912. Pulse (sitting) 96. Hands in bath at 3:14 p. m., in calorimeters at 3:27. At 3:40 right hand put into water at 42.8 C.

When taken out of the cold water the right hand was distinctly redder than the left. Cooling of calorimeters, R., 0.505 C. in forty-one minutes; L., 0.19 C. degree in sixteen minutes. Volume of right hand in calorimeter 367 c.c., of left hand 355 c.c. He is right-handed. Rectal temperature 37.35 C. Blood-pressure in right arm, systolic 108, 88 (sudden change in sound), 81 (sound gone). The left arm, systolic 108. (Table 18.)

TABLE 18.—CALORIMETRIC MEASUREMENTS IN CASE OF CHARLES H. SECOND EXAMINATION

Time	Right	Left	Room Temp. C.	Time	Left	Room Temp. C.	Notes
3:26	31.89	31.85	21.9	3:47	31.90	22.5	
3:28	31.85	31.81	22.0	3:48	31.91	22.4	
3:29	31.85	31.81	22.15	3:49	31.92	....	
3:30	31.85	31.81	22.15	3:50	31.925	22.8	
3:31	31.855	31.82	....	3:51	31.93	....	
3:32	31.86	31.825	22.4	3:52	31.935	22.9	
3:33	31.865	31.83	22.6	3:53	31.94	....	
3:34	31.87	31.84	22.8	3:54	31.945	22.7	
3:35	31.875	31.84	....	3:55	31.955	....	At 3:55 right hand put in water at 8.6 C.
3:36	31.88	31.85	22.6	3:56	31.955	....	
3:37	31.88	31.855	22.5	3:57	31.955	....	
3:38	31.895	31.86	....	3:58	31.955	....	The right hand is red. He feels the water very cold.
3:39	31.895	31.86	....	3:59	31.95	23.7	
3:40	31.895	31.865	....	4:00	31.945	....	
3:41	.....	31.875	23.0	4:01	31.94	23.5	
3:42	.....	31.875	....	4:02	31.94	....	The right hand does not now feel cold at all. Still red.
3:43	.....	31.875	22.8	4:03	31 94	....	
3:44	.....	31.88	....	4:04	31.935	23.7	
3:45	.....	31.885	22.7	4:05	31.93	....	Hand out of calor. at 4:05.
3:46	.....	31.89	....	4:21	31.74	....	4:21 temp. of R. is 31.39 C.

The distribution of the anesthesia and the history of the case seem to indicate that a nerve injury was the starting point of the vascular condition. The flow in the right foot was 0.51 gram per 100 c.c. per minute and in the left 1.35 grams, with room temperature 23.0 C. The flow in the right hand was 3.43 grams, and in the left hand 3.71 grams per 100 c.c. per minute, with room temperature 22.6 C. While, then, the flow in the hands is much below the normal, which corresponds well with the rather feeble action of the heart and with the patient's anemic condition, the flow in the left foot preserves a ratio to that in the hands not far from normal. The flow in the right foot, however, is distinctly poor, even in proportion to the poor hand flow. The cause accordingly of the small flow in the right foot is not a central one, but is local. This agrees well with the patient's observation that he cannot keep the right foot warm, and that the red color which it first exhibits when he stands becomes pale blue. The blood-flow measurement corroborates the conclusion that in the right foot the blood is stagnating in the capillaries of the engorged area.

SUMMARY

1. In cases with marked arteriosclerosis the blood-flow in the hands is smaller and the contralateral vasomotor reflexes less pronounced than normal.

2. In cases of thoracic aneurysm the flow in the hands may be normal. Where it is subnormal there is no evidence, apart from a unilateral deficiency in some cases due to the pressure of the aneurysm, that the existence of the aneurysm as such has any influence in diminishing the flow, the diminished flow being associated with coexisting pathological conditions (myocardial changes, valvular lesions).

3. A great difference in the form of the pulse-wave in the two radials associated with thoracic aneurysm does not necessarily indicate a difference in the flow through the hands. The hand flows may be identical when the sphygmograms from the radials on the two sides are very different.

4. In three cases of Raynaud's disease the hand flows were subnormal even in the absence of an actual attack, in the more advanced cases very much below the normal.

5. An abnormally great contralateral reflex vasoconstriction to cold seems to characterize the earlier stages of Raynaud's malady. When it has existed for a long time and gangrene has occurred, the vasomotor reactions indicate the existence of anatomical changes in the vessels, which do not permit vasomotor reflexes as intense as at first.

Case	Age	Date	Pulse Rate	Blood Pressure	Temperature (C.) of				Volume of Part in c.c	
					Room	Art Blood	Calorimeters		Right	Left
							Right	Left		
Chas. S....	69	7/ 8/13	80	180, (120)	28.3	36.3	30.70	30.75	437	410
					28.3	....	30.96	.....	.....	.....
					28.3	....	31.12	.....	.....	.....
Fred S.....	58	5/ 8/13	116	122, (101)* 63	23.8	36.9	31.28	31.25	497	484
					23.9	....	31.47	.....	.....	.....
					23.9	....	31.70	.....	.....	.....
					23.9	....	31.91	.....	.....	.....
					24.0	....	31.99	.....	.....	.....
					24.2	....	32.19	.....	.....	.....
Paul K...	57	4/24/12	100	115	22.8	37.5	31.14	31.27	454	451
					22.6	....	31.52	31.54	.....	.....
Joseph C..	50	1/31/11	88	160	21.5	37.2	29.49	29.43	505	480
Wm. B.....	53	12/22/10	84	205	20.8	37.1	28.81	28.97	410	390
		1/17/11	88	210	22.2	36.9	31.07	30.82	435	410
Richard B.	38	5/23/11	100	....	27.9	37.1	31.03	30.75	495	437
					28.0	....	.....	31.09	.....	.....
					28.0	....	.....	31.26	.....	.....
					28.1	....	.....	31.41	.....	.....
					28.2	....	.....	31.66	.....	.....
Sam S....	31	12/10/12	124	L.,118,(58) R.,157,(61)	22 2	37.9	31.98	32.01	580	603
John McL..	50	8/27/12	....	156, 83	22.2	36.15	30.73	30.72	498	475
					21.2	....	30.53	30.44	1,697	1,712
		8/28/12	97	....	21.1	36.7	30.63	30.59	507	454
					20.4	....	30.87	30.76	1,780	1,749
Mrs. W. G.	28	4/24/11	108	....	25.3	37.55	30.22	30 24	391	375
					25.1	....	30.51	.....	.....	.....
					25.0	....	30.73	.....	.....	.....
					....	....	30.77	.....	.....	.....
					2.66	....	30.87	.....	.....	.....
Mrs. C. B..	29	5/ 9/13	112	....	21.7	37.35	31.09	31.10	273	282
					22.3	....	31.10	31.27	.....	.....
					22.3	....	31.11	31.21	.....	.....
					22.8	....	31.14	.....	.....	.....
					22.9	....	31.19	.....	.....	.....
					22.8	....	31.24	.....	.....	.....
					22.7	....	31.25	.....	.....	.....
					22.7	....	31.30	.....	.....	.....
Maurice T.	41	4/17/11	92	....	25.7	36.5	29.84	29.76	470	466
					26.3	....	.....	30.11	.....	.....
					26.6	....	.....	30.22	.....	.....
					25.0	....	.....	30.34	.....	.....
					25.2	....	.....	30.59	.....	.....
Anthony P.	36	10/11/12	120	....	27.8	39.15	31.90	31.92	406	460
James P...	63	4/10/12	....	....	22.0	37.05	30.51	30.59	438	414
					22.0	....	.....	30.78	.....	.....
		4/11/12	68	....	25.6	37.35	30.92	30.93	1,090	1,175
K.	50	4/16/12	116	140, 100	23.8	36.7	30.55	30.65	352	310
					24.0	....	30.44	.....	.....	.....
		4/18/12	....	....	22.5	37.1	29.55	29.72	313	304
					20.3	37.0	30.13	30.26	950	985
					20.7	....	.....	30.67	.....	.....
					21.1	....	.....	30.84	.....	.....
Miss W...	25	5/ 9/11	88	....	24.1	37.6	30.13	30.05	292	298
					24.3	....	30.19	.....	.....	.....
					24.3	....	30.23	.....	.....	.....
					24.4	....	30.24	.....	.....	.....
Chas. H....	42	12/ 5/12	100	....	23.0	37.0	31.11	31.20	961	924
		12/10/12	96	108, (88) 81	22.6	36.8	31.87	31.84	367	355
					22.9	....	.....	31.87	.....	.....
					22.7	....	.....	31.92	.....	.....
					23.6	....	.....	31.93	.....	.....

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* As in the other papers, the numbers in brackets in this column give the pressure at which the sound had disappeared.

The condensed results of three of the cases referred to in this paper (Meyer, G., J. O'R. and this series (Heart, 1911, iii, 33)

Heat Given Off in Gram-Calories			Blood-Flow in Gm. Per Min.		Flow Per 100 c.c. of Part Per Min.		Notes
Right	Left	In Mins.	Right	Left	Right	Left	
930	822	8	23.07	20.57	5.25	5.01	Arteriosclerosis.
723	.....	8	18.81	.....	4.30	.....	Left hand in water at 8.5 C.
724	.....	7	22.18	.....	5.08	.....	Left hand in water at 43 C.
1,449	1,428	10	28.64	28.08	5.76	5.80	Arteriosclerosis.
410	.....	3	27.96	.....	5.62	.....	Left hand in water at 43 C.
1,790	.....	10	38.24	.....	7.69	.....	Left hand still in water at 43 C.
244	.....	3	18.18	.....	3.65	.....	Left hand in water at 8c.
731	.....	6	27.57	.....	5.54	.....	Left hand still in water at 8 c.
1,362	.....	10	32.13	.....	6.46	.....	Left hand in water at 38.5 C.
795	656	7	19.84	16.71	4.37	3.70	Aneurysm first seven minutes.
2,801	2,143	15	34.69	26.63	7.64	5.90	Last fifteen minutes in calorimeters.
2.580	2,460	11	33.81	31.09	6.69	6.66	Aortic aneurysm.
3,581	2,927	14	34.36	28.59	8.38	7.33	Thoracic aneurysm.
3.269	2,974	14	44.50	38.82	10.23	9.47	
3,247	2,239	11	54.03	35.62	10.91	8.15	Innominate aneurysm.
....	517	4	.....	23.89	.....	5.47	Right hand in water at 8.1 C.
....	792	4	.....	37.63	.....	8.61	Right hand still in water at 8.1 C.
....	413	3	.....	26.91	.....	6.16	Right hand in water at 4.3 C.
....	1,516	7	.....	44.23	.....	10.12	
4,466	4,292	13	64.47	62.28	11.11	10.32	Aortic aneurysm.
157	208	14	2.07	2.73	0.41	0.57	Cardio-renal disease with aneurysm.
114	100	8	2.81	2.43	0.17	0.14	Feet.
525	501	17	5.65	5.36	1.11	1.18	
616	608	10	11.74	11.37	0.66	0.65	Feet.
842	754	9	14.18	12.93	3.62	3.44	Raynaud's disease.
1,534	.....	12	20.18	.....	5.16	.....	Left hand in water at 43 C.
170	.....	3	9.23	.....	2.46	.....	Left hand in water at 12 C.
375	.....	4	15.36	.....	3.93	.....	Left hand still in water at 12 C.
477	.....	4	19.83	.....	5.07	.....	Left hand dried and wrapped.
298	299	8	6.61	6.64	2.42	2.35	Raynaud's disease first eight minutes.
795	1,079	16	8.83	12.12	3.23	4.29	Next sixteen minutes in calorimeters.
392	415	7	9.97	10.73	3.65	3.80	Last seven minutes of the sixteen.
200	.....	2	17.89	.....	6.55	.....	Left hand in water at 43 C.
651	.....	10	11.74	.....	4.30	.....	Left hand still in water at 43 C.
167	.....	2	15.18	.....	5.56	.....	Left hand in water at 12 C.
118	.....	2	10.74	.....	3.93	.....	Left hand still in water at 12 C.
477	.....	5	1,752	.....	6.41	.....	Left hand still in water at 12 C.
1,491	1,111	8	31.09	22.89	6.67	4.87	Arteritis in leg.
....	347	5	.....	12.07	.....	2.59	Right hand in water at 9 C.
....	589	4	.....	26.06	.....	5.59	Right hand still in water at 9 C.
....	382	3	.....	22.97	.....	4.93	Right hand in water at 43 C.
....	1,630	6	.....	51.09	.....	10.96	Right hand still in water at 43 C.
324	336	10	4.96	5.16	1.22	1.12	Gangrene of fingers; septic endocarditis.
1,033	1,199	15	11.59	13.75	2.65	3.32	Diabetes.
....	1,027	11	.....	16.54	.....	3.99	Right hand in water at 43 C.
2,023	2,858	23	15.19	21.50	1.39	1.83	Feet (left gangrenous).
95	87	18	0.95	0.88	0.27	0.28	Myocarditis; cyanosis. (Congenital heart?)
44	.....	10	0.78	.....	0.22	.....	Left hand in water at 41.8 C.
335	434	15	3.29	4.35	1.05	1.43	Cyanosis much less.
2,912	4,712	23	20.47	33.77	2.15	3.42	Feet (left toes gangrenous).
....	1,357	9	.....	26.46	.....	2.68	Right foot in water at 10.5 C.
....	1,726	11	.....	28.30	.....	2.87	Right foot in water at 42 C.
467	300	R 11 L 9	6.32	4.90	2.16	1.64	Purpura.
372	.....	8	6.97	.....	2.38	.....	Left hand in water at 43 C.
234	.....	7	5.04	.....	1.72	.....	Left hand in water at 9.1 C.
133	.....	4	5.04	.....	1.72	.....	Left hand dried and wrapped.
474	1,192	18	4.96	12.67	0.51	1.37	Feet (edema of right).
559	588	10	12.59	13.17	3.43	3.71	Hands.
....	210	4	.....	11.83	.....	3.33	Right hand in water at 42.8 C.
....	700	11	.....	14.49	.....	4.08	Right hand still in water at 42.8 C.
....	321	10	.....	7.32	.....	2.06	Right hand in water at 8.6 C.

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the abrupt change in the sound occurred; the smaller number following is the pressure at which

Margaret H.) are omitted from the table, having already been given in Table II, Paper I, of

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STUDIES ON THE CIRCULATION IN MAN*

THE BLOOD FLOW IN THE HANDS AND FEET IN NORMAL AND PATHOLOGICAL CASES

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FOR many purposes it is more important to know the rate at which the blood is flowing in an organ, the so-called mass movement of blood, than to know the pressure in the artery supplying the organ or part. The arterial pressure is not by itself a measure of the flow. With a high arterial pressure the flow may be small, with a low arterial pressure it may be large. For the rate of passage of the blood from arteries to veins obviously does not depend upon the arterial pressure alone, any more than the quantity of water which flows per minute along a pipe depends solely upon the height above the ground of the reservoir which feeds it. Two other factors of prime importance are concerned (the viscosity of the liquid itself being assumed to be constant): (*a*) the cross section of the pipe, (*b*) the height above the ground of the orifice from which the water escapes. (*a*) corresponds to the calibre of the vessels between artery and vein, (*b*) to the venous pressure.

At present we possess no method for measuring the blood flow which is at once simple enough and accurate enough for clinical purposes. I have accordingly worked out a method which permits the quantity of blood passing through a part like the hand to be easily determined with approximate accuracy. Changes produced in the flow by reflex vasomotor influences, especially those connected with changes in external temperature, by the application and withdrawal of a tourniquet or Bier's bandage, by alterations in the mechanics or chemistry of the respiration, as in forced breathing or the inhalation of oxygen, and by muscular exercise, have also been investigated in this way in normal and clinical cases.

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* Delivered November 23, 1912.

SECTION I. METHOD

The method depends upon the fact that the amount of heat produced by a part like the hand during rest is negligible in comparison with the heat conveyed to it by the arterial blood. If, then, we determine the amount of heat given off by the hand to a calorimeter in a given time, and know the temperature of the incoming (arterial) and of the outgoing (venous) blood, we can calculate how much blood must have passed through the hand in order that it might give off this amount of heat. The quantity of heat given off is estimated by putting the hand into a calorimeter such as is shown in Fig. 1.

It consists of an interior copper vessel containing a known amount of water (in the experiments usually about three litres), into which the hand is inserted through an orifice of appropriate size and shape in the lid, heat-tight closure being made by the collar of thick felt shown on the top of the calorimeter. The interior vessel is packed in broken cork in a larger outer vessel and the lid is covered with sheet cork to reduce as far as possible the loss of heat, and to protect the calorimeter against irregular cooling when exposed to draughts. The actual loss is estimated by separate experiments, and added to the amount of heat given off by the hand as indicated by the rise of temperature in the water. The hand is prepared for insertion into the calorimeter by a preliminary immersion, for not less than ten minutes, in a large bath containing water at approximately the same temperature as that in the calorimeter. The temperature of the water in the calorimeter is read on a thermometer permitting hundredths of degrees to be accurately estimated. The calorimeter is mounted on a stand which can be raised or lowered by a screw to permit its use either for a patient sitting in bed or for an ambulatory patient who is able to sit in the high chair shown in Fig. 2. As a general rule the flow in the two hands is simultaneously measured. The quantity of blood in grammes flowing through the hand in the time of the experiment is given by the formula: $Q = \frac{H}{T - T^1} \cdot \frac{1}{s}$ where Q is the quantity of blood, H the heat given off by the hand, T the temperature of the arterial blood, T^1 the temperature of the venous blood, and s the specific heat of blood. In estimating H the water equivalent of the hand itself (obtained by multiplying its volume by 0.8) and the water equivalent of the calorimeter (80 grammes) must be added to the quantity of heat corresponding to the actually observed rise of temperature. The specific heat of blood is taken at 0.9. Knowing the volume of the hand, we can express the flow in grammes per minute per 100 c.c. of hand substance. The volume of the hand is easily estimated by the amount of water which it displaces, when immersed in a glass douche can to the level to which it was inserted into the calorimeter. The douche can is connected by the tubulure to a burette, on the scale of which the vertical displacement of the water is read off. The amount of water which must be added to that in the can in order to give the same level in the burette is clearly the volume of the hand. The distance to which the hand is to be inserted into the calorimeter is fixed by making a horizontal mark with a pencil at the level of the lower border of the styloid process of the ulna. A parallel mark is drawn above this at a distance equal to the combined thickness of the felt collar and the lid of the calorimeter, and this second mark is just kept in view above the collar during the experiment. The lower mark must then define the limit up to which the hand is enclosed in the calorimeter. The collar is supported by a flange around the orifice. The temperature of the arterial blood at the wrist is taken as 0.5° below the rectal temperature, since this was the difference actually found in a normal person. It can be measured by determining that temperature of the calorimeter at which the hand neither gains nor loses heat. Where the rectal temperature cannot be conveniently obtained the mouth temperature is taken as that of the arterial blood at the wrist. The temperature of the venous blood is taken as the average temperature of the calorimeter during the experiment, since direct estimations of the temperature of blood collected by puncture of hand veins, during immersion of the hand in baths at known temperatures, showed that the excess of the temperature of the venous blood over that of the bath was so small as to be negligible for such bath temperatures as are used in the experiments. All details of these observations are omitted here. It may be remarked that since no account has been taken of the small excess of temperature of the venous blood over that of the calorimeter which must necessarily exist even in the superficial veins, the results cannot be too large, but may, on the contrary, be somewhat below the true values. This is important because for nearly all purposes it is much more useful to know the minimum flow below which the true flow cannot lie than to know the possible maximum flow. Some of the blood leaves the hand by deep veins, but the dimensions of the part and the anatomical situation of the vessels make it certain that no great error can be introduced by taking the temperature of the blood in the superficial veins as the average temperature of the whole of the blood as it leaves the hand.

The method for the measurement of the flow in the hands[1] was modified to suit the feet. This made it possible to make observations on persons who were too ill to sit in a chair for hand flow measurements.

Since the heat given off per 100 cubic centimeters of tissue per minute by the foot of a normal adult is considerably less than that given off by the hand, it was necessary to construct the interior vessel so that as small an amount of water as possible would suffice to immerse the foot completely.

TECHNIC OF FOOT FLOW MEASUREMENTS

In its final form the foot calorimeter consists of an interior oval vessel of tinned copper (Fig. 3) packed in broken cork in an outer vessel of galvanized iron. Both vessels are somewhat wider at the anterior (toe) end than at the posterior end. The top of the inner vessel has in it an oval opening somewhat wider at the anterior end. This opening, as is obvious from the shape of the foot, must be much larger than in the case of the hand calorimeter, and when the foot has been inserted it is partly closed by the removable copper lid shown at the right lower corner of the figure. The hole in this lid allows it to be lifted easily by the fingers. On the lid, once the foot is in position, lies the thick felt collar shown at the left of the figure. Inside the calorimeter the foot rests on thick copper wire netting, shown leaning against the front of the calorimeter. This allows the water to pass freely under the foot when it is stirred by the two goose feathers, the ends of which are seen protruding from the two openings, one on each side of the thermometer. The calorimeter in the figure is tilted so as to display the posterior end of the footrest lying in position on the bottom of the inner vessel. The anterior part of the top of the inner vessel slants down somewhat toward the front in order to reduce the capacity of the vessel without encroaching on the space needed for the toes. The thermometer is protected against contact with the patient's toes by a cylinder of copper perforated with numerous holes, which passes down through the top of the inner vessel to the level of the lower end of the bulb. The orifice for the introduction of the foot is surrounded by a flange on which the lid and the felt collar rest. Vertical rings of copper surround all the orifices so as to allow the top of the inner vessel to be covered, first with a layer of broken cork, and above that with sheet cork. The upper surface of the sheet cork is varnished.

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[1] Stewart, G. N.: Heart, 1911, iii, 33.

Fig. 4 shows the position of the patient with his feet in the calorimeters when he is well enough to sit in the high chair employed in the measurement of the flow in the hand. For the convenience of the observer the chair and the calorimeters are placed upon a platform so as to elevate the thermometers to a sufficient height above the floor to enable them to be read conveniently. By a simple method of fixation all possibility of slipping of the chair is prevented.

In the first experiments a horizontal pencil mark was drawn around the ankle, always bearing the same relation to the external malleolus, and above this a parallel line was drawn at a distance equal to the thickness of the felt collar plus the thickness of the flange. The height of the calorimeters was then adjusted so that the upper line just appeared above the felt collar, the patient sitting in the chair with his legs hanging down. The footrest inside the calorimeter was not used with this arrangement. It was found to be somewhat troublesome for the patient to maintain the same level throughout the experiment in this way. It was therefore decided to abandon it and to cause the patient to set his foot on the footrest. Before withdrawal of the foot a pencil line is now traced around the ankle just below the flange, or it may be traced above the collar, and after withdrawal of the foot a parallel line traced at a distance below the first line equal to the combined thickness of collar and flange. The object of the first procedure was to insure that in all experiments the foot should be inserted into the calorimeter to the same anatomical level, as was always done with the hands. In the case of the hands undoubtedly a fairer comparison of the flow in different individuals is obtained in this way than if the fingers were made in every case to touch the bottom of the calorimeter, since the inclusion of different proportions of the wrist and forearm would to some extent vitiate the results. From the shape of the foot, however, it is clear that the second procedure leads to a much smaller variation in the portion of the foot immersed than would be the case for the hand, since in the adult the variation in the vertical distance from the sole to a given anatomical point on the ankle is much less than the variation of the length of the hand,—from the tip of the middle finger to a fixed anatomical point on the wrist, for example. As a matter of fact, in the adult patients examined the variation in the distance between the flange and a fixed point on the external malleolus when the sole rested on the footrest was small. Any error in comparing the feet of different persons was further reduced by the fact that the difference of level affected the portion of the foot (the ankle) whose horizontal cross section was smallest. For very small feet, as those of children, an additional footrest which increased the space between the sole of the foot and the bottom of the calorimeter was employed. A great advantage of the footrest, in addition to the increased comfort of the patient, is the certainty that without any attention the foot remains at the same level within the calorimeter throughout the experiment. For particular purposes in the case of children or of adults with exceptionally small feet, it may sometimes be desirable, where accurate comparison is required with other cases, to revert to the first method, although, of course, for comparison of the flow in the feet of one and the same person at different times or under different conditions, this would offer no advantage.

The volume of the foot was measured by displacement in the same way as that of the hand. The oval copper vessel at the left of Fig. 4 was made for this purpose. The cross section of the vessel must be as small as possible in order to permit as large a change of level as possible in the attached burette. Where very large or very small feet are being investigated it is of advantage to have vessels of correspondingly different size.

When patients are not well enough to sit up in the chair the flow in the feet can be easily measured in the way shown in Fig. 5. The subject is lying on his back on a movable bed with his legs hanging over the foot of the bed. The height of the calorimeters is adjusted so that the soles of the feet rest on the footrest. No complaint of discomfort was made by any of the fever patients investigated in this way.

The technic of the preparatory bath is the same as that for the hands, except that instead of the patient putting his feet into the bath, the bath is generally slipped up over his feet. This is necessarily the case where patients are examined in bed. On account of the greater thickness of the feet, the period of immersion in the bath can advantageously be made longer than is necessary for the hands. For the same reason it is probable that the calculated results differ from the actual flow by a greater amount in the case of the feet than in the case of the hands. In both, of course, the observed flow establishes a minimum below which the actual flow cannot lie. It was pointed out in the previous communication that this follows from the principle of the method.

Another point of considerable importance is that the feet and legs, being less accustomed to exposure than the hands and arms, at least in temperate climates, greater precautions have to be taken to prevent vasoconstriction due to the exposure, especially of wet skin, to the air of the room. The legs are kept covered as far as possible down to the bath, and afterward down to the calorimeters. A somewhat higher bath temperature than that commonly employed for the hands is probably also advantageous for the foot measurements. The temperature of the arterial blood at the ankle is taken as 0.6° C. below the rectal temperature.

In general, measurements of the hand flow are to be preferred for obtaining information as to the condition of the circulation as a whole. It is in cases where the local conditions made it desirable to examine the foot flow, or where the patients were too ill to sit up for the hand examination, that foot flow measurements were undertaken. For the sake of comparison the hand flow was also measured wherever possible. It will be pointed out later that the ratio of the foot flow to the hand flow sometimes reveals interesting features.

SECTION II. RESULTS ON NORMAL PERSONS

A typical experiment on the feet and hands of M. C., a healthy man aged 24 years, height 5 feet 10 inches, weight 165 pounds, on whose hand flow numerous observations had been made, will illustrate the results obtained.

M. C., pulse (sitting) 98. Feet put into bath at 1.42 P.M. At 1.54 P.M. the subject lay down on his back. At 1.56 P.M. feet put into calorimeters. 2,775 c.c. of water in each calorimeter. The calorimeters as finally reduced in capacity were used.

Time.	Temperature (C.) of			Notes.
	Calorimeters.		Room.	
	Right.	Left.		
	degree	*degree*	*degree*	
1.58	30.87	30.88	24.3	
2.00	30.97	30.93	24.3	
2.02	31.06	31.01		From 2.04 to 2.06 stirring of left calorimeter insufficient.
2.04	31.18	31.14	24.3	
2.06	31.295	31.20		Pulse (lying down) 92.
2.08	31.43	31.39	24.3	
2.10	31.57	31.51		
2.12	31.70	31.65	24.1	
2.14	31.795	31.75		At 2.14 subject sat up and continued sitting for rest of experiment.
2.16	31.87	31.82	24.2	
2.18	31.92	31.91	24.3	
2.20	31.99	31.96		
2.22	32.08	32.04	24.6	
2.24	32.10	32.10		Stirring of right calorimeter insufficient for the last minute.
2.26	32.18	32.18	24.6	
2.28	32.23	32.25		
2.30	32.295	32.31	24.4	At 2.30 right foot put in water at 8° C.
2.32		32.37		
2.32½	32.32			

Time.	Temperature (C.) of Calorimeters. Right.	Temperature (C.) of Calorimeters. Left.	Temperature (C.) of Room.	Notes.
		degree	*degree*	
2.34		32.38	24.6	Subject says the left foot feels colder than before.
2.36		32.42	24.6	
2.38		32.465	24.6	
2.40		32.495		
2.42		32.54	24.6	
2.44		32.60		
2.46		32.68	24.6	
2.48		32.73		
2.50		32.78		At 2.50 right foot put in water at 43°.
2.52		32.80	24.6	
2.54		32.86		

Time.	Temperature (C.) of Left calorimeter.	Temperature (C.) of Room.	Notes.
	degree	*degree*	
2.56	32.905	24.6	
2.58	32.99		
3.00	33.095	24.7	
3.02	33.22		
3.03			Temperature of right calorimeter 31.80 degrees
3.04	33.31	24.6	
3.06	33.405		At 3.06 foot removed from calorimeter.
3.07	33.40		
3.18	33.17		Pulse (sitting) 97.

Cooling of right calorimeter 0.52° in 31½ minutes.

Cooling of left 0.23° in 11 minutes.

Volume of right foot 1,232 c.c., of left 1,195 c.c.

Hands put into bath at 3.40 P.M. Hands put into calorimeters at 3.52. 3,015 c.c. of water in each calorimeter.

Time.	Temperature (C.) of Calorimeters. Right.	Temperature (C.) of Calorimeters. Left.	Temperature (C.) of Room.	Notes.
	degree	*degree*	*degree*	
3.51½	31.10	31.22		
3.53	31.10	31.26		
3.54	31.18	31.32	24.3	
3.55	31.26	31.41		
3.56	31.35	31.50		
3.57	31.44	31.59		
3.58	31.53	31.67	24.3	
3.59	31.63	31.76		
4.00	31.72	31.81	24.3	
4.01	31.795	31.895		
4.02	31.87	31.98		At 4.02 left hand put in water at 8°C.
4.03	31.91		24.3	
4.04	31.98			
4.05	32.02		24.4	
4.06	32.08			
4.07	32.14		24.5	
4.08	32.21			
4.09	32.27		24.3	
4.10	32.31			

Time.	Temperature (C.) of Right calorimeter.	Temperature (C.) of Room.	Notes.
	degree	*degree*	
4.11	32.37		
4.12	32.43	24.4	
4.13	32.49		
4.14	32.53	24.3	
4.15	32.595		
4.16	32.67		At 4.16 left hand put in water at 43° C.
4.17	32.71	24.4	
4.18	32.74		
4.19	32.78		
4.20	32.83	24.25	
4.21	32.88		
4.22	32.93	24.35	
4.23	32.98		
4.24	33.03	24.3	
4.25	33.08		
4.26	33.125	24.3	
4.27	33.22		At 4.27 hand out of calorimeter.
4.53	32.90		Temp. of left calorimeter 31.40°.

Cooling of calorimeters, right 0.32° C. in 26 minutes; left 0.58° in 51 minutes. Volume of right hand 505 cubic centimeters, of left

485 cubic centimeters. Rectal temperature 37.1° C. Water equivalent of calorimeters with contents in feet observations, right 3,899, left 3,871. The corresponding numbers for the hand observations are, right 3,499, and left 3,483.

In this experiment the flow in the right foot was 5.11 grammes, and in the left 5.23 grammes per 100 cubic centimeters of foot per minute lying down, and only 3.96 grammes for the right, and 4.17 grammes for the left sitting up. In J. R., another normal young man, 20 years old, there was also a reduction in the flow in the sitting position, although less marked than in M. C. (from 7.98 and 7.58 grammes for the right and left foot, respectively, to 7.84 and 6.90 grammes per 100 cubic centimeters of foot per minute). This is of importance in connection with the fever observations, for it permits the assumption that the observed flows were at any rate as large as would have been obtained had the patients been sitting. These observations can therefore be safely compared with all the data obtained on normal persons. The flows in M. C. in this experiment agree with the results obtained nearly two years previously. This shows that when proper precautions are taken, the range of variation in the observed foot flow in one and the same healthy person is moderate, just as is the case for the hands. Therefore, when great differences, usually in the direction of deficiency, are found in pathological cases it can be assumed with some confidence that they are not due to accidental differences in the external conditions.

The reflex vasomotor effects from one foot to the other are similar to those obtained in the hands, only the constriction elicited by cold seems to be more durable. Thus in M. C. immersion of the right foot in water at 8° C. caused a diminution in the flow in the left foot from 4.17 to 3.12 grammes per 100 cubic centimeters per minute for the first ten minutes of the immersion. This gave place rather suddenly, as in the hand, to an increase in the flow (to 5.17 grammes per 100 cubic centimeters per minute) for the remaining eight minutes of the immersion. The greater susceptibility to vasoconstriction of the feet than of the hands has already been mentioned in connection with the technic of the measurement since it introduces a possibility of error which must be carefully minimized or excluded, especially in pathological cases, for in not a few clinical conditions this susceptibility seems to be augmented. Where organic local changes are excluded a marked diminution in the foot flow due to vasoconstriction can usually be discriminated from a feeble flow in the feet due to deficient driving power in the circulation, by comparing the flow in the hands under the same conditions. For M. C. this was done in the experiment under discussion. The flow in the hands in the sitting posture amounted to 14.71 grammes per 100 cubic centimeters per minute for the right, and 15.10 grammes for the left. Even the greatest foot flow seen in this individual does not approach one-half of the hand flow per 100 cubic centimeters of tissue per minute. The average of four experiments on different dates for the right foot in the sitting position is 4.28 grammes. The average of nine already published [2] experiments on the hands of M. C. in the sitting position, suitable as regards the range of room temperature and comparable in other respects, is 12.77 grammes for the right hand, and 12.29 grammes for the left.

In Table I are given the condensed results of nine additional experiments on M. C.'s hands, the average flow in which is 12.95 grammes for the right hand, and 12.41 grammes for the left. If the observations of May 24, 1911, and November 27, 1911, be excluded, as obviously extreme results due to external temperatures which for the conditions of our experiments may be considered extreme, we get an average of 12.91 grammes for the right hand, and 12.61 grammes for the left.

In this man, then, the ratio of 1 to 3 holds approximately for the hand and foot flow as determined under our conditions. It is not pretended that the deficiency in the foot flow as compared with the hand flow is in reality exactly as great as this. As already pointed out, the difference between the observed and the actual flow in the foot may be expected to be greater than the corresponding difference for the hand on account of the difference in the dimensions of the two parts. The smaller the

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[2] Stewart, G. N.: Heart, 1911, iii, 33.

TABLE I.

	Date.	Age in years.	Pulse rate.	Blood pressure.	Temperature (C.) of				Volume of part in c.c.		Heat given off in small calories			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.											
							Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
Normal Individuals.																		
M. C. Hands.	May 4, 1911	22	90		*degree* 23.3	*degree* 36.7	*degree* 30.04	*degree* 30.03	486	470	3,380	2,950	9	62.48	54.60	12.86	11.61	L. forearm bandaged before experiment and bandage removed.
	May 24, 1911		87		27.0	36.8	30.91	30.91	470	457	3,228	2,976	7	86.99	80.20	18.51	17.55	
	Nov. 2, 1911		76		22.2	36.5	29.78	29.77	465	435	884	878	3	48.72	48.31	10.48	11.10	Cuff on right arm, but no pressure.
	Nov. 3, 1911		88	115	25.1	36.75	30.01	30.04	493	459	1,815	1,627	5	59.84	53.88	12.14	11.74	Cuff on right arm, but no pressure.
	Nov. 9, 1911		87	115	24.1	36.7	30.84	30.88	465	465	2,357	2,046	7	63.84	55.80	13.73	12.0	Flow in left hand, 12.54 allowing for swelling.
	Nov. 15, 1911		—	113, 85	25.2	36.8	30.79	30.83	480	461	2,932	2,737	8	67.53	63.68	14.07	13.81	
	Nov. 27, 1911		100	124	21.4	36.9	29.92	29.87	477	455	1,617	1,356	7	36.77	30.57	7.71	6.72	
	Dec. 11, 1911		74	122, (92), 82	24.5	36.6	31.18	31.12	450	444	2,315	2,225	8½	55.83	53.17	12.41	11.98	
	Mar. 26, 1913	24	97		24.5	36.6	31.53	31.61	505	485	2,712	2,612	8	74.29	73.28	14.71	15.10	
					24.5		32.27				3,289		14	60.24		11.93		L. hand in cold water.
					24.6		32.73				507		3	48.52		9.60		L. hand in warm water.
					24.5		33.10				1,889		8	74.96		14.84		L. hand still in warm water.
M. C. Feet.	May 2, 1911	22			25.25	36.8	30.38		1,220		1,510		6	43.55		3.57		Foot at rest.
					25.4		30.55				1,253		5	44.55		3.65		Working foot.
					25.2		30.71				1,437		6	43.69		3.58		Foot at rest.
	May 18, 1911		76		26.4	36.9	31.42		1,210		2,116		10	42.90		3.54		
	June 17, 1911		84		21.8	37.0	30.60	30.26	1,170	1,085	3,988	3,346	12	57.69	45.97	4.93	4.24	
	Mar. 26, 1913	24	92		24.5	36.5	31.38	31.34	1,232	1,195	4,064	4,064	14	62.99	62.50	5.11	5.23	Lying on back.
			98		24.5		32.06	32.03			3,119	3,212	16	48.78	49.90	3.96	4.17	Sitting.
					24.6			32.46				1,355	10		37.26		3.12	R. foot in cold water.
					24.6			32.76				1,664	8		61.79		5.17	R. foot still in cold water.
					24.6			32.84				930	6		47.05		3.93	R. foot in warm water.
					24.6			33.16				2,747	10		91.38		7.64	R. foot still in warm water.

TABLE I.—*Continued.*

	Date.	Age in years.	Pulse rate.	Blood pressure.	Temperature (C.) of				Volume of part in c.c.		Heat given off in small calories			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.											
							Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
						Normal Individuals.												
					degree	*degree*	*degree*	*degree*										
C. B. Hands.	May 22, 1911	22	80		28.9	36.6	31.15	31.21	415	410	3,975	4,176	16	50.65	53.83	12.20	13.13	
					29.0		31.76				497		4	28.52		6.95		L. hand in cold water.
					29.0		31.96				1,028		6	41.03		9.89		L. hand still in cold water.
					29.1		32.36				2,022		11	48.17		11.60		L. hand in warm water.
	Nov. 17, 1911		106	103	24.9	36.5	30.15	30.29	430	424	2,338	2,712	8½	49.22	57.09	11.45[1]	13.46[1]	
	Nov. 20, 1911			113	24.8	36.45	30.68	30.66	410	405	1,369	1,334	10	26.36	25.55	6.43[1]	6.30[1]	
	Nov. 21, 1911		104	115	24.2	36.75	31.28	31.36	410	405	2,096	2,060	9	47.30	46.83	11.54[1]	11.42[1]	
	Nov. 24, 1911		80	116	23.5	36.6	30.48	30.40	400	385	785	953	6	23.56	28.46	5.89[1]	7.39[1]	Hands felt cold though not to the subject.
C. B. Foot	May 2, 1911		72		26.3	36.3	30.02		980		1,573		6	46.38		4.73		Foot at rest.
					26.3		30.20				1,145		4	52.14		5.32		Working foot.
					26.0		30.36				1,216		4	56.82		5.79		Foot at rest.
J. R. Hands.	Mar. 22, 1913[2]	20	52		24.0	36.0	30.90	30.88	397	354	2,388	1,537	13	40.02	25.66	10.08	7.25	
					24.2		31.30				1,092		13	19.85		5.00		L. hand in cold water.
					23.95		31.42				113		2	13.70		3.45		L. hand in warm water.
					23.9		31.49				409		3	33.59		8.46		L. hand still in warm water.
					23.95		31.72				1,610		7	59.70		15.04		L. hand still in warm water.
	Mar. 25, 1913		62	101, 60	24.8	36.5	31.62	31.55	393	376	3,206	2,217	15	48.66	33.17	12.38	8.82	
					24.4		32.11				460		5	23.28		5.92		L. hand in cold water.
					24.4		32.25				802		5	41.93		10.67		L. hand still in cold water.
					24.4		32.37				347		3	31.11		7.91		L. hand in warm water.
					24.5		32.61				1,699		7	69.32		17.64		L. hand still in warm water.
J. R. Feet.	Mar. 25, 1913		76		25.1	36.4	31.54	31.40	1,008	959	4,925	4,580	14	80.42	72.70	7.98	7.58	Lying on back.
					24.6		32.60	32.34			4,869	4,359	18	79.09	66.27	7.84	6.90	Sitting.
					24.5			32.87				1,440	10		45.32		4.72	R. foot in cold water.
					24.45			33.08				1,405	8		58.77		6.12	R. foot in warm water.
					24.45			33.35				1,753	8		79.82		8.27	R. foot still in warm water.

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[1] The cuffs of the sphygmomanometer were on the arms, but were not inflated.

[2] In preparing the lecture for publication some observations made since it was delivered **have** been included.

TABLE I.—*Continued.*

	Date.	Age in years.	Pulse rate.	Blood pressure.	Temperature (C.) of				Volume of part in c.c.		Heat given off in small calories			Blood flow per min. in gm.		Flow per 100 c.c. of part per min.		Notes.
					Room.	Arterial blood.	Calorimeters.											
							Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
					Normal Individuals.													
					degree	*degree*	*degree*	*degree*										
N. R.	Apr. 8, 1913	8¾	84		24.0	36.7	30.97	31.10	203	181	1,292	1,226	15	16.70	16.21	8.22	8.95	Hands.
					24.0	36.6	30.98	30.88	491	480	1,509	1,272	18	16.57	13.72	3.37	2.86	Feet.
					Fever Patients.													
					degree	*degree*	*degree*	*degree*										
F. B.	Dec. 5, 1912	53½	92	104, 58	23.0	38.8	31.62	31.80	1,081	1,044	2,176	2,273	15	22.45	24.05	2.07	2.30	Pneumonia. Feet.
	Dec. 11, 1912		112		22.0	38.7	31.24	31.11	1,072	1,023	2,059	1,646	21	14.63	11.47	1.36	1.12	
J. B.	Oct. 2, 1912	24	108	100, 78	24.4	38.75	31.21	31.38	927	945	3,382	3,840	16	31.15	36.18	3.36	3.82	Typhoid. Feet.
	Oct. 8, 1912		104	109, 65	22.2	38.85	30.36	30.35	924	900	—	—	—	—	—	—	—[3]	
	Oct. 16, 1912		106	104, 66	23.0	39.6	30.50	30.58	834	837	547	502	10	6.68	6.18	0.80	0.74	
	Nov. 1, 1912		87	108, 84	22.2	36.85	30.32	30.34	780	740	1,531	1,306	16	16.28	14.04	2.08	1.89	
M. V.	Oct. 8, 1912	29	108	118, 89	22.2	39.9	30.97	30.86	1,322	1,294	2,292	2,211	14	20.37	19.41	1.54	1.50	Typhoid. Feet.
	Nov. 5, 1912		80	107, (92) 65	22.9	37.35	30.80	30.82	1,109	1,100	1,145	1,272	14	13.82	15.45	1.24	1.40	
F. S.	Oct. 2, 1912	28	72	100, (77), 58	24.1	37.3	31.77	31.59	1,295	1,258	2,180	2,076	23	19.04	17.56	1.47	1.39	Typhoid. Feet.
F. D.	Oct. 1, 1912	26	81	108, 84	22.9	36.7	31.91	31.88	425	423	1,511	1,426	9	38.94	36.50	9.16	8.63	Typhoid (convalescent). Hands, feet.
					22.45	36.6	30.90	30.82	1,135	1,117	910	787	16	11.08	9.45	0.98	0.85	
J.McD.	May 16, 1912	26	80		23.2	36.7	31.28	31.52	511	505	3,118	3,568	18	35.51	42.52	6.95	8.42	Typhoid (convalescent). Hands.
					23.2			31.99				654	5		30.83		6.10	R. hand in cold water.
					23.1			32.14				833	5		40.59		8.04	R. hand still in cold water.
					23.3			32.34				1,242	10		31.65		6.26	R. hand in warm water.

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[3] The flow was so small that even after the feet had been in the calorimeters for 21½ minutes the loss of heat by the calorimeters to the room was not yet balanced. The feet were withdrawn before usable readings were obtained. From the readings obtained it is practically certain that the foot flow was not greater than on October 16.

foot the closer must the observed come to the actual flow. Yet the error due to this is apparently not great, as is indicated by the comparison of the hand and foot flows in a boy, N. R., 8 years and 9 months old. The observations on him were made for the purpose of testing this point. The volume of his feet is no greater than that of M. C.'s hands, in fact somewhat less, and the average thickness of the skin even including that of the soles is probably less. Although the greatest thickness of the boy's foot is probably somewhat greater than the maximum thickness of M. C.'s hand, the dimensions of the two objects do not differ sufficiently to forbid the assumption that the equalization of temperature of the boy's foot and the man's hand with that of the calorimeter would be about equally complete. If then the flow in the adult foot as estimated in this method were much below the actual flow, the measured flow in the boy's foot should approach much nearer to that in his hand than is the case in the adult. Yet the ratio was practically the same as in M. C.

From all the observations on the foot flow the following conclusions seem permissible.

1. The blood flow in the foot is smaller per unit of volume of the part than in the hand, the ratio of foot flow to hand flow per 100 cubic centimeters of the part usually ranging in normal persons from 1 to 3 and 1 to 2.

2. In the supine position, with the legs hanging down, the flow in the feet seems to be somewhat greater than in the sitting position.

The changes produced in the flow in normal persons by changes in the physiological condition of the part, or in the external temperature, or by mechanical interference with the circulation, can be readily followed by this method. The higher the room temperature, the greater in general is the flow. When this factor is taken into account the results on different days, with similar calorimeter temperatures, in one and the same individual, leading a uniform life, do not differ greatly, although different individuals when tested under apparently similar conditions show a much greater range in the blood flow. Some normal persons know and say that their hands are habitually cool or cold, others that their hands are habitually warm. The former will have a relatively small and the latter a relatively large flow of blood in the hands as estimated by this method.

The influence of muscular contraction in increasing the flow is easily demonstrated. Thus with a calorimeter temperature of about 24.38° C. and 23.64° C. for the right and left hand respectively and a room temperature of 21° C., the flow was 15.4 grammes per 100 c.c. per minute for the right hand while it was being made to contract in the calorimeter and only 4.9 grammes for the left, which remained at rest. Since 4.9 grammes is a much smaller flow than was ever found in this person, M. C., with both hands at rest, the increased flow in the contracting right hand is accompanied by a diminished flow in the contralateral hand.

The diminution in the flow caused by a moderate degree of obstruction to the venous circulation (a rubber band constricting the wrist, but not very tightly) can also be very simply measured. Thus, in an experiment on one of the normal persons, the flow in the left hand, which had been 13.2 grammes and 13.1 grammes per 100 c.c. per minute in two experiments immediately preceding the constriction, was diminished to 4.2 grammes per 100 c.c. per minute for the first four minutes after constriction. For the next six minutes the flow rose to 9.3 grammes per 100 c.c. per minute, owing, of course, to the gradual increase of the venous pressure distal to the band, which enabled the obstruction to be more and more successfully overcome. The high initial flow observed in this person was due to two factors, (*a*) a relatively high room temperature (24° C.), (*b*) the fact that the cutaneous circulation of this individual is habitually copious.

In another experiment (on M. C.) in which the upper arm was compressed on the right side by inflation of the cuff of an Erlanger sphygmomanometer, the flow for the right hand fell from 8.74 grammes to 4.52 grammes per 100 c.c. per minute. The initial flow was unquestionably diminished somewhat, even by the application of the cuff, without inflation, for at the same time the flow in the left hand was 10.83 grammes per 100 c.c. per minute.

In this connection may be mentioned experiments in which the flow was tested in a normal man, M. C., after bandaging one hand so as to cause temporary anæmia of the part, or after bandaging of one forearm so as to cause temporary congestion of the hand. In both cases the bandage was removed just before the hands were put into the calorimeters.

In an experiment in which the left hand had been rendered anæmic the calculated flow was 7.45 grammes per 100 c.c. of hand per minute for the left hand, against 6.26 grammes for the right. In an experiment in which the left hand had been rendered passively congested the calculated flow was 11.61 grammes per 100 c.c. per minute for the left hand and 12.86 grammes for the right for the first nine minutes in the calorimeters. For the second nine minutes the flows were respectively 10.96 grammes and 13.78 grammes for the left and right hands.

Certain questions connected with the clinical measurement of blood pressure may also be investigated by this method. For instance, it was concluded, on the basis of observations on two healthy young men, that a pressure equal to the systolic pressure, as estimated by the clinical methods used, applied to the upper arm by a broad cuff, causes complete cessation of the blood flow in the hand. Since the pressure in the veins distal to the constricting armlet eventually becomes equal to the systolic arterial pressure, this was taken to mean that the lumen of the arteries under the cuff is actually obliterated, a question concerning which there was some doubt. From the same investigation the following points were also determined.

1. When the pressure in an armlet compressing the upper arm is reduced from the systolic arterial pressure the blood flow in the corresponding hand is only slightly increased for a considerable decrement of pressure.

2. The pressure in the armlet must fall somewhat below the "diastolic" pressure, as clinically determined, before any marked increase in the flow through the hand occurs.

3. The first decrements of pressure below this "critical" pressure are accompanied by a much greater increase in the flow through the hand than further equal decrements.

4. A handicap of half the "diastolic" pressure causes only a relatively small diminution in the flow through the hand; and

it was suggested that the method of handicapping the circulation in the arm or leg by known pressures and observing in what degree the handicap is overcome, may in certain cases constitute a useful supplementary method of clinical investigation.

The influence of direct heating of the hand (high bath and calorimeter temperatures) in increasing the flow is also followed without difficulty. Thus, in three experiments on the same person with calorimeter temperatures above that of the arterial blood the flows were, without exception, the greatest measured in the whole series of observations, viz.: 16.3 grammes per 100 c.c. per minute with calorimeter temperature 39.6° C., 16.5 grammes with calorimeter temperature 41.5°, and 18.3 grammes with calorimeter temperature 39.09° C., all for the left hand. Where the calorimeter temperature is above that of the arterial blood the blood abstracts heat from the calorimeter, instead of giving off heat to it, and it is from the *fall* of temperature in the water (corrected of course for the loss of heat to the surroundings) that the flow has to be calculated.

The effect of forced breathing on the blood flow in the hand was tested in two normal persons. It was found to distinctly diminish it. The increase in the respiratory movements was by no means excessive. Yet in one case, M. C., the flow fell from 12.66 grammes to 8.62 grammes per 100 c.c. of hand per minute for the right hand and from 12.76 grammes to 9.20 grammes for the left hand, to rise again when breathing became normal. In the other case, C. B., the relative change was even greater although the initial flow was less. It would lead us too far to discuss here the significance of this result. One might think of the acapnia caused by the washing out of the carbon dioxid as a possible influence. Mechanical changes in the thorax, and particularly those affecting the filling and discharge of the heart, must also be taken into account. One moral to be drawn is that while the respiratory pump plays a part of some consequence in the normal movement of the blood, and may even become the preponderant factor when the heart and the vasomotor mechanisms are crippled, the idea of the "deep-breathing" fanatics that voluntary interference with the exquisitely regulated respiratory mechanics *must* be good receives no support, at least so far as the circulation in the periphery is concerned.

Coming now to the observations on clinical cases, a few general remarks may be of use.

General Remarks.—The material studied consisted of patients in the Dispensary of Western Reserve University and Lakeside Hospital, and the private practice of friends. The major portion of the material was from the wards of the City and other hospitals. Comparable results are much more easily obtained in successive observations on hospital patients whose surroundings and regimen are fairly constant, and fewer precautions necessary than on dispensary or private patients. In particular the influence of the external temperature, the factor which of all others among the external conditions is most apt to influence results, is much more easily controlled in the case of the hospital patients, especially in winter. The observations on the latter were made in a room in the hospital to which the patients were brought in the wheel chair, or the movable bed, or to which if well enough they walked. As is true for many kinds of physiological clinical examination the observations are more satisfactorily made in a separate room than in the open wards. Where the external conditions are controlled and the clinical state of the patient has not altered noticeably, the results of the blood flow measurements from day to day, and, indeed, from week to week, show a very fair and often a surprising degree of constancy. Not only is the hospital patient in a temperature which varies comparatively little, but his diet is also controlled and the general regimen under which he lives is relatively stable. In any of the hospital cases the approximate constancy of the flow was not only seen in one and the same hand, but also in the proportion between the flows in the two hands where a conspicuous difference existed. As regards the dispensary material, care had to be taken in winter that the person was long enough in the room before the observations were begun, especially if he came to the dispensary with bare hands. It is true that if the flow were immediately measured a result would be obtained which would give the flow correctly enough for the given condition of the hands but it would be useless as an expression of the flow under the approximately standard conditions which have to be established if comparison of the flow in the same patient at different times or in different patients is proposed. In summer the factor of external temperature presents no difficulty in dealing with dispensary patients.

SECTION III. OBSERVATIONS IN CASES WITH OBVIOUS DIFFERENCES BETWEEN THE TWO HANDS OR FEET

In addition to the clinical interest which attaches to the measurements in the individual cases dealt with in this section, the material was chosen partly as a test of the technic of the method, as in many of the cases the qualitative difference between the two sides could be foreseen from the anatomical difference which existed.

In a man 21 years old, with healing burns on both hands but more extensive on the right, the flow was 7.04 grammes per 100 c.c. per minute for the right hand and 5.44 grammes for the left hand (for the last nine minutes in the calorimeters) with an average room temperature of 25° C. The burned areas on both hands were quite red, and taking the whole surface of the hands into account the vascularity of the superficial layers must have been considerably greater in the right than in the left hand. In both hands many blood-vessels in the new tissue must be nearer the surface than in the normal hand, a point of interest in connection with the technic of the method (Heart, 1911, iii, 55). In spite of the red color both hands felt rather cold to the touch, and this agrees perfectly with the tardiness with which the thermometers rose at first and with the calculated blood flow, which for the man's age and the room temperature is subnormal. The redness is due to the number of capillaries in the healing areas and to the fact that they lie just under the surface, not to a great flow of blood through widely dilated vessels. The case presented an opportunity for studying the flow in blood-vessels which have not long existed and whose vasomotor connections may be still incomplete or immature. Immersion of the left hand in warm water caused a marked increase, and subsequent immersion of the left hand in cold water a marked decrease in the flow in the right hand. The persistence of both reflexes was remarkable. Another peculiarity observed in only one other case, in which one of the hand nerves had been divided and had not apparently completely regenerated, was that the temperature of the right hand calorimeter during the immersion of the left hand in the warm or cold water showed abrupt changes; for instance, a sudden rise of the thermometer between the third and fourth minutes of immersion of the left hand in the cold water. The patient denied that his hand ever touched the thermometer, and from the position of the thermometer in the calorimeter contact of the hand with it can scarcely occur unless the hand is executing extensive groping movements of which there was no sign in these observations. The most plausible explanation of the phenomenon would seem to be that in the new blood-vessels, although the vasomotor connections had been established, there is still an abnormal vasomotor instability. The intensity of the total reaction may be due either to hyperexcitability of the receptive surfaces of the left hand (afferent path) or to hyperexcitability of the newly formed vasomotor endings, including the muscle of the new blood-vessels (efferent path), or to both.

In a man 42 years old, suffering from a malignant tumor of the right forearm (with metastases), with some œdema of the forearm down to the wrist, the flow in the right hand was 4.69 grammes per 100 c.c. of hand per minute, in the left hand 5.13 grammes, with an average room temperature of 23.2° C. The right hand was not swollen, as shown by the measurement of its volume. The deficiency in the right hand was an actual deficiency and not merely an apparent one, owing to the reckoning in of œdema liquid in the volume of the hand, since by measurement the right hand was only 3 c.c. larger than the left. It is therefore probable that the deficiency was due to the interference of the tumor with the venous return from the hand. In so far as it was not connected with inflammatory changes, the œdema was also probably caused by interference with the venous flow. In certain cases the blood flow measurement might help to settle the question whether œdema is due to obstruction on the lymph path or on the venous path. Obstruction confined to the lymphatics might cause œdema without diminution in the blood flow. Where a tumor is confined to the bone, obstruction to the flow of blood in the hand may be expected to be less marked than where it has extensively invaded the soft tissues.

A condition where œdema coincided with obstruction to the lymph flow not involving the venous flow seems to have been realized in the case of Charles B., a man 47 years old, in whom the diagnosis of Hodgkin's disease was made. He entered the hospital with both legs and feet greatly swollen. The swelling was stationary and little, if at all, diminished in the morning. During his entire stay in the hospital the swelling of the legs remained unchanged. There was no œdema elsewhere and no evidence of any lesion of the heart or kidneys. He had always lived in Cleveland. All the palpable lymph glands were enlarged. The blood flow in the right foot was 2.34 grammes per 100 c.c. of foot per minute, or allowing for the œdema fluid 3.04 grammes, and in the left foot, 2.50 grammes (allowing for the œdema fluid 3.24 grammes), with average room temperature of 22.7° C. These flows are by no means small for the feet. Indeed, in comparison with the hand flows (2.82 grammes for the right and 3.22 grammes for the left hand) they are quite large. A certain degree of anæmia, some cyanosis and dyspnœa were present, and this may contribute to the small hand flow (Stewart, Journal of Experimental Medicine, 1913, xviii, No. 2). It may be supposed that this would tell equally on the blood flow through the feet, but, in the absence of special observations on this point, we cannot be certain whether the compensatory vasoconstriction in anæmia is not greater in the anterior limb than in the posterior limb. It is conceivable that the circulation in the anterior limb has a closer association with the pulmonary circuit than the circulation in the posterior limb. That the hands were exceptionally liable to vasoconstriction was shown by separate observations, which gave a still smaller flow. It is rare to find a case in which the flow per 100 c.c. of foot per minute comes out as great as the flow per 100 c.c. of hand per minute in the same individual. In the vast majority of clinical cases the hand flow greatly preponderates, and this is the invariable rule for normal persons so far as our experience goes (Journal of Experimental Medicine, 1913, xviii, p. 354).

Interference with the local circulation would seem to be excluded in this case as a cause of the œdema of the legs. It is more likely, indeed, if we take account of the hand flows that there is a local acceleration of the blood flow in the legs, perhaps through partial paralysis of their vasoconstrictors by the pressure of the same masses if mechanical pressure is responsible for the œdema. If we confine ourselves to the question, leaving out all other possibilities, whether the œdema is dependent on venous or on lymphatic obstruction the blood flow measurements give an answer unequivocally in favor of lymphatic obstruction, to this extent supporting the diagnosis of Hodgkin's disease.

Charles W., a man aged 42 years, a clerk, admitted to City Hospital October 29, 1912, had rheumatism at the age of 8 years, since which time the left leg seemed to be weaker and smaller than the right. At that time the arms and legs were somewhat swollen and extremely sensitive. He had a "stroke of paralysis" in 1903. Both arms and legs were affected. In seven months he had recovered from the stroke and had no trouble in walking or otherwise until 1907, when he had a second stroke. It took four years for his complete recovery from the second attack. Four months before admission he fell on the sidewalk and abraded the left shin about three inches. It healed somewhat. It kept partially healing and opening again and the pain continued so that he could not sleep. There are many petechial spots on left leg. Reflexes increased in the left leg. The left leg is atrophied and much smaller than the right and one and a half inches shorter. The left foot is not small, although doubtless smaller than the right. It is the lower leg which is conspicuously small.

I was asked to make an examination of the flow in the feet. The flow in the right foot was 1.89 grammes per 100 c.c. per minute and in the left 1.72 grammes with average room temperature 23.9° C. From this practical equality it was concluded that there was no obstruction in the main arterial supply of the left leg which could account for the slow healing of the sore and for the pain in the leg. If the cause was vascular it was therefore a vasomotor affair. Undue susceptibility to vasoconstriction might account for the relatively small flow in both feet. The slow increase in the flow in the left foot at the beginning of the observations supports the view that it was peculiarly susceptible to vasoconstriction. The cause of the small flow was not a central one (deficiency in the driving power of the heart), since the flow in the hands was normal (10.62 grammes for the right per 100 c.c. per minute and 10.00 grammes for the left with room temperature 23.9° C.).

On discharge he was able to use the left foot better than for seven years.

Some interesting cases in which obvious differences between the two hands exist were found in unilateral inflammations. Of these we shall cite three: one in which the inflammation was due to an infected finger, one in which it was due to gout, and a third in which it was due to a sprain.

A man, aged 34, had an infection of the right hand with considerable swelling and redness; otherwise he was in good health. The protocol has been already published (Heart, 1911, iii, p. 82). The flow was 11.93 grammes per 100 c.c. per minute, or allowing for the œdema fluid 13.05 grammes in the right hand against 4.92 grammes in the left, with room temperature 23.8°. There can be no doubt that along with an increase in the flow in the inflamed hand in this case there goes a decrease in the flow in the normal hand, since 4.92 grammes is an abnormally small flow for a healthy man of this age. The suggestion is that in order to provide for the increased flow in the infected area a vasoconstriction, possibly elicited reflexly through the pain nerves of the infected hand, is brought about elsewhere and particularly in the symmetrically placed parts on the opposite side.

However this may be, a fact of great interest is elicited when the vasomotor reflexes from the left to the right hand are studied. Immersion of the left hand in cold water caused scarcely any reduction of the flow in the right hand (from 11.93 to 11.15 grammes, or allowing for the œdema liquid, from 13.05 grammes to 12.20 grammes). This is a very much smaller reaction than normal and suggests that vasoconstrictor impulses to the inflamed part are blocked; or, possibly, vasodilator impulses favored, perhaps by a local action on the vasomotor nerve endings of the bacterial products or of something produced in the reaction between them and the leucocytes. It is clear that such a block may be of importance in maintaining against casual and vagrant vasoconstrictor impulses, so to say, the full stream of blood which is so important a factor in combating the infection.

Immersion of the left hand in warm water also caused hardly any increase in the flow through the right hand beyond promptly removing the small effect of the cold water. But this is of less interest, as the vasodilatation in the infected hand was probably already nearly maximum, and it is usual to obtain a relatively small reflex vasodilatation in a hand with a large initial flow. It is, however, again of interest that the initial vasoconstriction which normally follows immersion of the contralateral hand in warm water is here absent, a further indication of a block on the vasoconstrictor path. A very different picture is presented by the case of gouty (non-bacterial) inflammation in which two examinations were obtained.

The patient was a man aged 50 years. He had suffered from gout for twenty years. There were tophi in the scrotum as well as in the ears. The right wrist and hand were swollen and painful.

At the first examination, on April 3, 1912, with room temperature 24.3° C. the flow was 6.88 grammes per 100 c.c. of hand per minute, or allowing for the swelling 7.47 grammes in the right hand and 3.07 grammes in the left. Immersion of the left hand in warm water caused the usual diminution of the flow in the right; to 4.66 grammes (allowing for swelling 5.06 grammes), followed by an increase to 9.88 grammes (or allowing for the œdema 10.73 grammes), a good vasodilatation. It must, of course, be remembered that the initial flow in the right hand did not correspond with anything like a maximal vasodilatation. It is therefore all the more significant that immersion of the left hand in cold water caused a marked and persistent decline of the flow in the right hand to 3.84 grammes (or allowing for the swelling to 4.16 grammes). There is then in this case of non-bacterial inflammation no sign of vasoconstrictor block.

The same fact comes out fully as well in the second examination (July 9, 1912), which was made on a very warm day with a room temperature of 29.7° C. The right hand was much more swollen at the second examination than at the first. At neither examination was there any pain in the left hand. The initial flow was 13.27 grammes (taking only the flow corrected for the œdema liquid) in the right and 8.13 grammes in the left hand. As compared with the previous examination, the flow in the left hand is of course proportionately more increased by the high external temperature than that in the right. It is still, however, for the temperature a distinctly subnormal flow. On immersion of the left hand in cold water, the flow in the right was diminished to 8.47 grammes, a very fair reaction in the normal direction, and this flow mounted to 12.82 grammes, nearly the initial flow, on subsequent immersion of the left hand in warm water.

It would not be profitable to speculate upon the reasons for the difference in the reflex vasomotor reactions in the two cases related further than to point out that the local infection is an acute affair, a bacterial invasion fraught with imminent peril to the organism if it be not promptly dealt with. The mechanism exists, and in the blood, for the effective and rapid destruction of the bacteria. On the other hand, if the essential condition of the gouty paroxysm be the deposition of urates in the tissue, while an increase in the blood stream may doubtless be of value in aiding the tissue to segregate the deposit so as to minimize its action as a mechanical irritant, no increase in the blood flow however great and however sustained will soon effect the re-solution of the deposit, which in any case is quite indifferent to the body as a whole and exposes it to no danger of invasion.

The third case was that of a man aged 66 years, who had sprained the little finger of his left hand three days before the examination. The hand was swollen but not greatly. He said the pain had diminished. The difference in flow between the two hands was very striking (1.7 grammes per 100 c.c. per minute for the right hand and 5.2 grammes for the left with a room temperature of 23.4° C.). The flow is small in both hands, which is accounted for by the arteriosclerosis (see Paper XI of this Series, Archives of Internal Medicine, 1913), the renal disease, and the age of the patient. It may be worth pointing out once more that a high systolic arterial pressure such as existed in this patient, far from indicating a copious flow, is commonly the index of a high peripheral resistance coupled with a small flow.

No observations were made on the vasomotor reflexes, although it would have been interesting to compare this case of traumatic non-bacterial inflammation with one of infection. The complicating conditions, however, especially the arteriosclerosis which tends to prevent marked vasomotor reflexes, rendered the case an unfavorable one for these tests.

Among the most interesting cases in this section are certain instances in which congenital or at least very long standing anatomical defects existed in one hand without markedly affecting its functional power. Here, as was to be expected, no great difference in the flow per 100 c.c. of hand was made out.

A girl 21 years old, who works with a sewing machine in a factory, came to the Dispensary for ''nervousness.'' She has suffered much from headache the past two or three months. Her left wrist is deformed, the styloid process of the ulna being very prominent, and the left hand is considerably smaller than the right. This difference is possibly due to rheumatism, but she has had it a long time, perhaps even from birth. The left hand is normally formed and she uses it in all ways in which a normal hand would be used, only it is not so strong as the right hand. The left anterior limb is shorter than the right and the girth of the forearm is distinctly less to the eye. The left hand does not get cold any more than the right and does not require to be better protected in winter. The pulse at the wrist is of fair volume to the finger.

With the rather high room temperature of 26° C. the flow in the right hand was 9.08 grammes per 100 c.c. of hand per minute, in the left 8.81 grammes.

A man aged 46 years, with spastic paralysis of the left wrist (birth palsy), showed a flow in the left hand but little less than that in the right (right hand 10.71 grammes per 100 c.c. per minute, left hand 10.2 grammes with room temperature 20.5° C.). These flows are perfectly normal. He uses the left hand largely in his work, that of a telegraph operator. It was obviously well supplied with blood.

A girl, 15 years old, congenitally deficient in intellect, was brought on this account to the Dispensary by her mother. Her left hand is congenitally defective, the thumb being wanting; otherwise it is perfectly formed, though small. The left arm, both upper and lower, is much smaller in girth than the right, and the elbow-joint appears very prominent between the two ill-developed segments. The left hand easily gets cold in winter. She uses it quite freely but not so much as the right. The whole left anterior extremity is somewhat shorter than the right.

With room temperature 26.5° C. the flow in the right hand was 5.96 grammes per 100 c.c. per minute, and in the left 6.6 grammes per 100 c.c. per minute. The flow in the defective hand is thus somewhat greater than in the normal one in contrast to the condition in a case of infantile paralysis in a boy 9 years and 6 months old, whose left hand was much atrophied and functionally of little use. In his right hand the flow was 15.0 grammes per 100 c.c. of hand per minute against 7.6 grammes in the left hand with room temperature 23.4° C.

A man aged 51 years had suffered amputation of the whole middle finger and the second and third phalanges of the index finger of the left hand for an injury. The proportion of skin in the left hand was thus considerably reduced. I have shown that the flow in the distal half of the hand is much greater per unit of volume than in the whole hand. It was to be expected, therefore, that the flow in the left hand in this case should be decidedly less than in the right. The expectation was realized, the flow in the right hand being 7.20 grammes and in the left 5.34 grammes with room temperature 24.5° C. The flow in the right hand is probably subnormal, as the patient had pulmonary tuberculosis with right pleural effusion, which had been aspirated two days before the examination (see p. 148).

The last case to be mentioned in this section is that of a woman 68 years old in whom Dr. Carl Hamann had ligated the innominate and right common carotid arteries for aneurism of the subclavian artery with a successful result. A month after the operation the blood flow in the two hands was compared on two successive days. No pulse could be felt in the right wrist or over the course of the right brachial. She says the right hand gets cold if left uncovered with the bed-clothes.

On being emptied, by stripping, the veins on the back of the right hand fill slowly from below. The right hand can execute all movements, but it is weak. There is some paræsthesia (pins and needles and numbness) in the right hand, but this she had before the operation, and it has not been intensified since. The nails on the right hand are getting clubbed. She has noticed that they are getting "like those of a man." The change in the nails was present before the operation, but is now more marked.

The calculated blood flow at the first examination was 5.32 grammes per 100 c.c. per minute for the left hand and 1.50 grammes for the right (ratio of right to left 1: 3.54). The next day the flows were 5.85 grammes and 1.68 grammes per 100 c.c. per minute for the left and right hands respectively (ratio 1: 3.48). Immersion of the left hand in warm water produced practically no effect on the flow in the right. It is obvious from the anatomical conditions that dilatation of the vessels of the right hand, even if it occurred, could scarcely aid the scanty collateral flow.[3]

SECTION IV. THE ANÆMIAS

Anæmia has a special influence, which it is essential to make clear, on the flow in the peripheral parts. Therefore, a number of clinical cases illustrating the anæmias will next be taken up.

The common characteristic of the anæmias as regards this point is a small flow in the hands as compared with a normal person of similar age and under similar external conditions. Thus in H. W., a case of pernicious anæmia with an erythrocyte count of 2,000,000 in a man 24 years old and with room temperature 23.5° C., the flow was only 2.06 grammes per 100 c.c. of hand per minute for the right hand, and 1.82 grammes for the left—*i.e.*, only one-third to one-sixth the amount to be expected in a healthy man of the same age under like conditions.

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[3] Four months later the flow in the right hand had improved so much that the ratio of right to left was 1: 1.3 and the vasomotor reaction from left to right hand was distinct. It was concluded that certain symptoms were not due to anæmia of the right hand and arm but to pressure of callus on the brachial plexus and that a further operation for their relief was therefore not contra-indicated.

In another case of pernicious anæmia, D. K., in a man 44 years old, the flow on an extremely hot day with room temperature 29.1° C. rose to 8.35 grammes per 100 c.c. per minute for the right hand, and 8.38 grammes for the left, whereas in the healthy young man, M. C., already referred to, the flows were respectively 17.98 grammes and 16.65 grammes with room temperature 27.1° C. In health, so far as our observations go, the flow is not inferior at the age of forty-four years to that at the age of twenty-two. The room temperature was one of the highest worked with in the whole series of observations and the calorimeter temperature was also relatively high. There is of course a cutaneous vasodilatation in response to the high external temperature, else life would be endangered, yet the hand flow in D. K. remains markedly subnormal. It is perfectly intelligible that under these conditions the further reflex vasodilatation under the influence of warm water applied to the contralateral hand is feeble, the flow increasing only to 9.10 grammes per 100 cubic centimeters per minute, while the reflex to cold is intense, the flow diminishing to 2.85 grammes. Blood examination gave erythrocytes 1,648,000, hæmoglobin 45 per cent., color index 1.4. The erythrocytes showed marked variation in size, polychromatophilia; punctate basophilic cells; nucleated reds.

In a case of marked secondary anæmia, S. K. (erythrocytes 2,112,000, hæmoglobin 45 per cent.), associated with carcinoma of the uterus in a woman forty-eight years old, the flow was only 1.26 grammes per 100 cubic centimeters of hand for the right, and 1.18 grammes for the left hand (for the last ten minutes in the calorimeters) with a room temperature of 23.3° C. She died 11 weeks later.

In a young man of 22 years, F. W., the subject of hæmophilia, the flow was 5.04 grammes per 100 cubic centimeters per minute for the right hand and 3.94 grammes for the left (for the last fifteen minutes in the calorimeters) with room temperature at 24.7° C. The flow was scarcely at all increased reflexly by the application of warm water to the contralateral hand, although it was easily decreased in the case of the right hand to 2.79 grammes per 100 cubic centimeters per minute by the application of cold water to the left hand. At the time of the blood flow examination there had been no hemorrhage for six weeks.

In Mrs. M. A., a woman 38 years old, with an erythrocyte count of 3,000,000 and a hæmoglobin percentage of 80, in whom a diagnosis of cirrhosis of the liver was made, the flow was 4.70 grammes per 100 cubic centimeters per minute in the right hand, and 5.44 grammes in the left hand (for the last thirteen minutes in the calorimeters) with room temperature 23.1° C., a flow below the normal for her age. The tardiness with which the point was reached at which the thermometers began to rise uniformly, indicating stubborn vasoconstriction, well illustrates a common characteristic of this group of cases. The consequence of this tardiness is that if we reckon the blood flow for a period of twenty-two minutes it comes out only 4.02 grammes per 100 cubic centimeters per minute for the right hand and 4.64 grammes for the left.

In three cases of the chlorotic type the flow although probably below the normal was by no means scanty. Thus in E. D., a girl of 16 years with an erythrocyte count of 4,100,000 and a hæmoglobin percentage of 50, the flow in the right hand was 6.25 grammes per 100 cubic centimeters per minute, and in the left 5.76 grammes (for the last thirteen minutes in the calorimeters) with room temperature 22.2° C. The contralateral vasodilatation produced by warmth was slight, the contralateral vasoconstriction produced by cold much more distinct.

In A. P., who are still nursing completely her 13-months-old baby, the red cell count was 4,600,000; the hæmoglobin 70 per cent., the flow in the right hand 8.75 grammes per 100 cubic centimeters per minute, and in the left 8.09 grammes with room temperature 23.5° C.

In Mrs. T., a woman aged 30 years, with an erythrocyte count of 4,584,000 and a hæmoglobin percentage of only 40, the flow in the right hand was 6.48 grammes per 100 cubic centimeters per minute and in the left 7.20 grammes with room temperature 22.6° C.

In a case of anæmia secondary to copious gastric hemorrhage in O. L., a man aged 36 years, the erythrocyte count was 2,250,000, the hæmoglobin percentage 45, the flow in the right hand 7.02 grammes per 100 cubic centimeters per minute, and in the left 6.90 grammes, with a room temperature of 25.4° C. For the age of this man and the relatively high room temperature, these figures are rather small, but very much higher than in H. W. and S. K., where the anæmia is associated with much graver general changes than in O. L., whose blood changes were probably at this time conditioned mainly or entirely by the hemorrhage. The contralateral vasodilatation to warmth was good, the flow in the right hand being increased from 7.02 grammes to 9.93 grammes per 100 cubic centimeters per minute when the left hand was immersed in warm water after the usual preliminary diminution (to 5.95 grammes). The reaction to cold was fair.

More than two years from the time of the first large hemorrhage he was still alive, but an inoperable carcinoma of the cardia had been found.

In a case convalescing from scurvy, J. B., a man 34 years old, the flow in the right hand was 5.53 grammes per 100 cubic centimeters per minute, and in the left 6.30 grammes, with room temperature 23.9° C. The vasomotor reflexes were good, the flow in the right hand increasing to 10.47 grammes (after a preliminary dip to 2.54 grammes for the first minute), when the left was immersed in warm water, and sinking to 5.66 grammes for the first three minutes of immersion of the left hand in cold water. For the two minutes succeeding the first minute of immersion of the left hand in cold water the flow in the right was only 4.68 grammes per 100 cubic centimeters of hand per minute.

On admission to the hospital three weeks before the blood flow examination was made the hæmoglobin was 60 per cent.

Finally, in a case of severe nose-bleed, in G. L., a man 26 years old, otherwise in good health and without symptoms, the flow was normal (10.27 grammes per 100 cubic centimeters per minute for the right hand, and 10.40 grammes for the left) with room temperature 24.2° C. The erythrocyte count was 4,256,000.

Plesch has stated that the output of the left ventricle per minute (the minute volume), measured by a gasometric method, is increased in the cases of anæmia investigated by him, including pernicious anæmia, chlorosis, and secondary anæmias. His explanation is that the deficiency of hæmoglobin entails the circulation of a greater quantity of blood through the lungs in order that the oxygen requirement of the body may be filled. He does not discuss the mechanism by which this necessary increase in the minute volume is obtained. My observations on the hand flow indicate in an interesting manner that an important, if not the sole, way in which the increased minute volume of the heart is rendered possible is the diminution in the flow through the periphery by vasoconstriction. This obviously will shorten the average circulation time of the blood and permit its quicker return to the right heart and therefore its more rapid circulation through the lungs. It is to be expected that the cutaneous vessels should be particularly affected by this vasoconstriction. For in the main the blood circulates in the skin, not in the interests of the nutrition of the skin itself, for which a comparatively small flow would suffice, but to regulate the loss of heat. Where it is important that the blood should pass in a fuller stream than ordinary through the lungs it can accordingly be readily spared from the peripheral layers of the body. Since the metabolism in the anæmic body is usually less than normal, a smaller cutaneous circulation than normal is in any case required to eliminate the heat produced. If the peripheral vasoconstriction is accompanied by a vasodilatation in the deeper and shorter vascular paths, especially in those passing through the viscera in which a free circulation must be steadily maintained if the metabolism is to proceed normally, the increase in the minute volume of the heart may be all the more easily secured. Although it may be that the doctrine of reciprocal innervation of the periphery and the deeper parts cannot now be maintained in any very thoroughgoing fashion, there is no question that reciprocal relations can and do exist. The relatively low blood pressure, in many of these cases, shows, in so far as it does not depend upon cardiac weakness, that the vasomotor block is not universal. Where the total volume of the blood is increased, as in chlorosis, the increased minute volume of the heart necessitated by the deficiency in hæmoglobin may be obtained with little if any diminution in the flow through the skin. For example, if the blood volume were doubled and the hæmoglobin percentage halved, the total hæmoglobin would be unaltered. It might then be possible that without diminution in the flow through the peripheral parts, the flow through the lungs could be doubled and the oxygen requirement completely met. In this case the quantity of hæmoglobin passing through the hand, per unit of time, might be reduced to one-half without change in the blood flow, while the quantity of hæmoglobin passing through the lungs would remain normal. In E. D., for example, the hæmoglobin passing through 100 c.c. of hand per minute would correspond only to that contained in three grammes of normal blood, a very marked deficiency in the hæmoglobin circulation through the hands for a girl of 16. In O. L., also, the apparently fair flow of about seven grammes of blood per 100 cubic centimeters of hand corresponds to the hæmoglobin of only about three grammes of blood normally rich in hæmoglobin.

In Mrs. A. P., whose hand blood flow appears to be normal (8.4 grammes per 100 cubic centimeters per minute for the average of the two hands), the hæmoglobin going through 100 c.c. of hand per minute is equivalent only to that contained in about six grammes of normal blood, a distinct although a not very great deficiency.

We shall not discuss the question whether an increase in the minute volume of the heart in the anæmias is not obtained in part or chiefly by an acceleration in its rate. For an increase in minute volume occasioned in this way would equally affect the peripheral circulation unless a redistribution of the blood were brought about by vasomotor action in the manner already suggested. Besides, considerable difference of opinion exists among observers as to the effect of changes in the rate of the heart on its output, and as to the changes in the output which are possible.

A glance at Table II (pages 123, 124) in which the results in the cases of anæmia are summarized, shows clearly that there is no direct relation between the pulse rate and the blood flow through the hand. The highest pulse rate of the series, 120 in H. W., was associated with one of the lowest hand flows, the lowest pulse rate, 52 in J. B., with a fair although subnormal flow. The independence of the hand flow and the pulse rate in different cases is still better displayed in Table III (page 125), embodying the results on a case of bradycardia, a case diagnosed as paroxysmal tachycardia, a case showing jaundice with a slow pulse, and a case showing jaundice with normal or somewhat accelerated pulse rate.

In the first blood flow examination in the case of bradycardia, X., with a pulse rate of 35 the flow was 10.37 grammes per 100 cubic centimeters per minute in the right hand, and 10.93 grammes in the left hand, with a room temperature of 24.7° C. A week later, with a somewhat higher average pulse rate and a room temperature of 24.5° C., the flows were respectively 8.75 grammes and 8.32 grammes. On the first day he had in accordance with his usual custom for some time taken no lunch, and had rested for a while after coming to the hospital. On the second day he had had lunch and was examined immediately on his arrival. The case was one of true bradycardia, not of heart block, the jugular tracing showing a number of *a* waves equal to the number of beats in the radial artery.

In Table III is next shown a case, F. R., a woman aged 52, with a pulse rate of 156 and a blood blow of only 4.78 grammes per 100 cubic centimeters per minute for the right hand, and 4.30 grammes for the left, although the room temperature was 26° C. This pulse rate indicates complete or almost complete inactivity of the inhibitory mechanism. It is of interest as a sign of concomitant inactivity, as regards reflex changes, of the vasomotor centres that the flow in one hand is practically unaffected by the application of heat or cold to the contralateral hand. So slight a reflex effect as that witnessed in this patient is seldom seen.

The third case in Table III, G. V., a man 44 years old, with long-standing jaundice (8 years) and a pulse rate of 63, had a flow in the right hand of only 2.69 grammes per 100 cubic centimeters per minute, and in the left 2.62 grammes, with room temperature 22.1° C. Anæmia was probably a factor in the small peripheral flow. His hands were always cold to the touch. Whether the continued itching of the skin of which he complained was concerned in the vasoconstriction is unknown.

In S. L., a case of jaundice (diagnosis, hypertrophic biliary cirrhosis) with a normal pulse rate, or perhaps a rate somewhat accelerated, the flow in the hands was even greater than normal for the room temperature of 21.7° C.,—14.86 grammes per 100 cubic centimeters per minute for the right hand, and 14.78 grammes for the left. An increase in the hand flow in disease is much less common than a decrease. The vasomotor reflexes were marked. The increased vasodilatation in the right hand (whose blood-vessels must have been already considerably dilated) on immersing the left hand in warm water is especially notable. The flow increased to 15.63 grammes per 100 cubic centimeters per minute. Immersion of the left hand in cold water caused a transient diminution of the flow in the right (to 9.05 grammes for the first two minutes), followed by an increase to 14.14 grammes per 100 cubic centimeters per minute for the remaining eight minutes of immersion.

In concluding this section of the lecture it is worth pointing out, perhaps, that if in anæmia peripheral vasoconstriction, especially in the cutaneous vessels, is a compensatory mechanism for increasing the stream of blood in the lungs, disorders of the skin caused or perpetuated by deficient circulation are rationally treated by measures which augment the hæmoglobin content of the blood. When the deficiency of hæmoglobin is remedied the deficiency in the cutaneous blood flow will take care of itself. It has long been known and is a commonplace of practice that many skin conditions are benefited by general treatment of the co-existing anæmia where local treatment alone is inefficacious. Local treatment of limited portions of the skin, however, aimed at increasing the blood flow there, would not be contraindicated from the point of view of the compensatory action of a general peripheral vasoconstriction. For vasodilatation in a limited area of the skin, while it might greatly benefit the local condition, would not appreciably affect the pulmonary flow.

In one and the same healthy individual and in pathological cases where the clinical state has undergone no sensible change, the hand flow varies only within narrow limits when the subject is under a steady regimen, and the controllable external conditions are the same. Where anæmia fever (p. 122) and possibly some other conditions (p. 148) are excluded it is probable that the hand flow is an index to the minute volume of the heart, and gives the means in successive observations of following to some extent changes in the minute volume. When the hand flow is not below the normal we can almost always conclude that the heart output is not less than normal (p. 133). The fact then that X., with a pulse rate of 35, had a hand flow entirely within the normal range for his age may be taken to indicate that his minute volume under the given external conditions was not less than normal. The output per beat must, therefore, have been twice that of a normal man of the same weight. Nothing, of course, can be said from these observations as to the power of his heart to respond to such increased requirements as occur during considerable muscular exertion. Miss Buchanan has remarked that among athletes at Oxford (rowing men) very slow pulse rates are not incompatible with great physical exertion.

CONCLUSIONS OF SECTION IV

1. In the cases of anæmia studied (pernicious anæmia, chlorosis, and secondary anæmia) the blood flow in the hand is smaller than the normal flow.

2. Accepting Plesch's result, that the minute volume of the heart is increased in the anæmias, the diminution in the hand flow is interpreted as a token of a vasoconstriction in peripheral parts which facilitates the increased flow through the lungs.

3. The deficiency in the hand flow is less in the chlorotic group than in the other cases of anæmia. The explanation suggested is that the increased total volume of the blood in chlorosis

permits the normal amount of hæmoglobin to circulate through the lungs without entailing a marked increase in the vasoconstriction of the peripheral parts.

4. The view that the diminution in the cutaneous blood flow in anæmia is a necessary compensatory arrangement for increasing the flow through the lungs affords a natural explanation of the beneficial effect in many cutaneous disorders of general measures, especially those aimed at improving the quality of the blood.

5. In a case of bradycardia with a pulse rate permanently below 40 during rest in a sitting position, the hand flow was normal.

SECTION V. THE BLOOD FLOW (MAINLY IN THE FEET) IN FEVER

In spite of much discussion we possess but little exact knowledge of the changes in the cutaneous circulation in fever, which constitute an essential, probably the chief, factor in the derangement of the temperature-regulating mechanism. I have endeavored to make a small contribution to our data by measuring approximately the blood flow in the feet in a number of cases of typhoid fever and in one case of pneumonia. Of one of the cases of typhoid four examinations were made in the course of a month. In a second case a similar program was planned but had to be modified on account of hemorrhage, and only two examinations were carried out. These, however, happened to be at the most interesting stages in the course of the fever. For comparison three cases at different stages in convalescence were investigated, each on one occasion. In the pneumonia case two examinations were secured, the last one four days before the death of the patient. The first of the typhoid patients, F. D., was far enough advanced in convalescence to permit him to sit up in a chair for the examination of the hands.

Here the hand flow lies within the normal range, being 9.16 grammes per 100 cubic centimeters per minute for the right hand, and 8.63 grammes for the left, with room temperature 23° C. The foot flow is much below the normal (0.98 grammes

TABLE II.

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature (C.) of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per min.		Flow per 100 c.c. of hand per min.		Notes.
					Room.	Arterial blood.	Calorimeters.		Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
							Right.	Left.										
					degree	*degree*	*degree*	*degree*										
H. W.	24	April 18,1911	120		23.5	37.5	30.19	30.20	412	378	931	753	17	8.49	6.88	2.06	1.82	Pernicious anæmia. R. B. C. 2,000,000.
D. K.	44	July 2, 1912	84	103, (82)60[1]	29.1	37.7	32.05	32.03	480	476	3,670	3,667	18	40.09	39.92	8.35	8.38	Pernicious anæmia. R. B. C. 1,648,000. Hæmoglobin 45.
					29.2		32.54				191		3	13.70		2.85		Left hand in cold water.
							32.67				957		7	30.20		6.29		Left hand still in cold water.
							32.80				192		2	21.79		4.54		L. hand in warm water.
							33.00				1,478		8	43.67		9.10		Left hand still in warm water.
S. K.	48	Jan. 24, 1913	108		23.3	37.15	31.17	31.14	330	324	225	208	10	4.18	3.84	1.26	1.18	Carcinoma. R. B. C. 2,112,000. Hæmoglobin 45.
F. W.	22	Dec. 27, 1912	100	124,73	24.7	36.75	31.55	31.45	449	403	1,589	1,145	15	22.63	16.00	5.04	3.94	Hæmophilia.
					24.2		31.80				1,126		11	22.97		5.11		Left hand in warm water.
					24.2		31.92				539		11	11.27		2.79		Left hand in cold water.
Mrs.M.A.	38	Jan. 28, 1913	80	118,(85)[1]	23.1	36.85	31.17	31.15	330	332	1,031	1,206	13	15.51	18.08	4.70	5.44	R. B. C. 3,000,000. Hæmoglobin 80.
E. D.	16	Feb. 5, 1912	130 96	105,(85)73	22.2	37.0	31.21	31.19	303	275	1,285	1,077	13	18.96	15.84	6.25	5.76	Chlorosis. R. B. C. 4,100,000. Hæmoglobin 50.
					22.5		31.32				320		5	12.51		4.12		Left hand in warm water.
					22.4		31.40				930		9	20.50		6.76		Left hand still in warm water.
Mrs. A. P.	32	Feb. 4, 1913	104 88	115,63	23.5	37.0	31.12	31.03	390	386	1,806	1,678	10	34.12	31.23	8.75	8.09	R. B. C. 4,600,000. Hæmoglobin 70.
Mrs. T.	30	Jan. 11, 1911	72		22.6	37.6	30.58	30.55	275	245	1,466	1,456	13	17.84	17.65	6.48	7.20	R. B. C. 4,584,000. Hæmoglobin 40.

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[1] The numbers in parentheses are the pressures determined by the auscultatory method at which the abrupt decline in the sound occurred; the smaller numbers following are the pressures at which the sound disappeared.

TABLE II.—*Continued.*

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature (C.) of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per min.		Flow per 100 c.c. of hand per min.		Notes.
					Room.	Arterial blood.	Calorimeters. Right.	Calorimeters. Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
					degree	*degree*	*degree*	*degree*										
O. L.	36	Apr. 27, 1911	96		25.4	37.3	29.64	29.58	470	448	2,048	1,934	9	33.00	30.93	7.02	6.90	Gastric hemorrhage. R. B. C. 2,250,000. Hæmoglobin 45.
					25.4		29.95				555		3	27.97		5.95		Left hand in warm water.
					25.4		30.20				1,492		5	46.69		9.93		Left hand still in warm water.
					25.4		30.47				798		5	25.96		5.52		Left hand in cold water.
					25.3		30.65				764		4	31.91		6.79		Left hand still in cold water.
					25.3		30.86				1,076		6	30.94		6.58		Left hand dried and wrapped.
J. B.	34	Apr. 4, 1912	52		23.9	36.7	30.63	30.67	407	410	1,231	1,403	10	22.53	25.85	5.53	6.30	Scurvy.
							30.79				55		1	10.34		2.54		Left hand in warm water.
					23.9		30.99				1,642		7½	42.60		10.47		Left hand still in warm water.
							31.21				342		3	23.07		5.66		Left hand in cold water.
							31.42				1,573		8	41.39		10.17		Left hand still in cold water.
							31.61				205		2	22.37		5.50		Left hand dried and wrapped.
							31.71				684		3	50.77		12.47		Left hand still wrapped up.
G. L.	26	Nov. 7, 1912	112	128,(110)86	24.2	38.2	31.93	31.83	362	360	2,098	2,148	10	37.18	37.46	10.27	10.40	Nose-bleed. R. B. C. 4,256,000.

TABLE III.

Case.	Age in yrs.	Date.	Pulse rate.	Blood pressure.	Temperature (C.) of				Hand volume in c.c.		Heat given off in small calories.			Blood flow in gm. per min.		Flow per 100 c.c. of hand per min.		Notes.
					Room.	Arterial blood.	Calori-meters.											
							Right.	Left.	Right.	Left.	Right.	Left.	In min.	Right.	Left.	Right.	Left.	
					degree	*degree*	*degree*	*degree*										
X.	32½	June 4, 1912	35		24.7	36.7	31.62	31.60	493	469	3,506	3,531	15	51.12	51.28	10.37	10.93	After rest. No lunch.
		June 11, 1912	51,35		24.5	37.0	31.60	31.47	477	444	3,650	3,312	18	41.72	36.97	8.75	8.32	After lunch, without rest.
Mrs. F. R.	52	May 25, 1911	156		26.0	38.1	30.12	30.03	326	335	1,007	942	9	15.58	14.41	4.78	4.30	
							30.35				940		8	16.84		5.16		Left hand in warm water.
							30.58				1,040		10	15.36		4.71		Left hand in cold water.
G. V.	44	Sept. 27, 1912	63	105,69	22.1	37.1	31.04	30.98	473	467	1,320	1,284	19	12.73	12.27	2.69	2.62	
S. L.	35	Jan. 8, 1913	84	117,(100)80	21.7	36.75	31.77	31.69	494	467	4,938	4,718	15	73.45	69.06	14.86	14.78	
					22.4		32.40				350		2	44.70		9.05		Left hand in cold water.
					22.2		32.66				2,058		8	69.88		14.14		Left hand still in cold water.
					22.1		33.16				2,495		10	77.22		15.63		Left hand in warm water.

per 100 cubic centimeters per minute for the right, and 0.85 grammes for the left). The ratio of the combined foot flows to the combined hand flows (1 to 9.7) is much too small and indicates clearly an abnormal sensitiveness of the feet to vasoconstriction, the exciting cause being probably the necessary exposure of the feet to the air and water. We shall see that there is evidence in the foot flows of abnormally great cutaneous vasoconstriction in all the typhoid cases examined, and at all stages of the fever which happened to coincide with an examination. This tendency to vasoconstriction seems to be carried into convalescence.

In the case of J. McD., who was still further advanced in convalescence than F. D., the prolonged reflex vasoconstriction, not followed by any vasodilatation in the left hand when the right was immersed in warm water, might be interpreted in the same way, as also the marked inferiority of the flow in the right hand as compared with the left. Such differences between the two hands in the absence of any known anatomical cause are apt to be observed in persons who exhibit other evidences of nervous, including vasomotor, instability.

Hyperexcitability of the vasoconstrictor mechanisms of the periphery is most naturally interpreted as a defensive reaction of the organism by which an increased supply of blood is afforded for those internal organs which bear the brunt of the infection. The fact that the blood pressure is low and the pulse dicrotic in spite of the constriction of the vessels of the periphery, indicates that other vascular paths, especially the splanchnic area, are more widely opened than usual. The fever, the rise of temperature of the internal parts and of the blood, may be considered as, in the main, a secondary and inevitable, and perhaps in itself an unimportant consequence of a sustained cutaneous vasoconstriction. When the temperature has risen to a certain height a balance between heat production and heat loss is necessarily again reached in spite of the vasoconstriction. Indeed, were the circulation in the skin entirely stopped it is clear that such a balance must also be eventually reached by augmentation of the flow of heat by conduction from the deeper parts.

It must be remembered that with a normal flow through the skin in fever the amount of heat given off would be greater than normal on account of the higher temperature of the blood. Table IV illustrates this point. Thus, while the amount of heat given off per 100 cubic centimeters of foot per minute in all the fever cases does not rise beyond the range for the normal persons, the amount of heat given off per gramme of blood passing through the foot is much greater in fever than with normal body temperature. And it is precisely when the flow of blood is small and the rectal temperature high that the heat loss per gramme of blood is greatest. Thus in J. B. on October 16, 1912, with rectal temperature 40.2° C., and in M. V. on October 8, 1912, with rectal temperature 40.5° C., over eight small

TABLE IV.

Case.	Date.	Heat given off per min. in small calories.		Heat given off per 100 c.c. of foot per min.		Heat given off per gm. of blood.		Rectal temperature. C.
		Right.	Left.	Right.	Left.	Right.	Left.	
				Normal Individuals.				
M. C.	May 2, 1911	251.6	—	20.6	—	5.77	—	*degree* 37.4
	May 18, 1911	211.6	—	17.4	—	4.93	—	37.5
	June 17, 1911	332.3	278.8	28.4	25.6	5.76	6.06	37.6
	Mar. 26, 1913	290.2	290.2	23.5	24.2	4.60	4.64	37.1
C. B.	May 2, 1911	262.1	—	26.7	—	5.65	—	36.9
J. R.	Mar. 25, 1913	351.7	327.1	34.8	34.1	4.37	4.49	37.0
N. R.	Apr. 8, 1913	83.8	70.6	17.0	14.7	5.05	5.14	37.2
				Fever Patients.				
F. B.	Dec. 5, 1912	145.0	151.5	13.4	14.5	6.41	6.29	*degree* 39.4
	Dec. 11, 1912	98.0	78.4	9.1	7.6	6.69	6.83	39.3
J. B.	Oct. 2, 1912	211.3	240.0	22.7	25.3	6.78	6.63	39.35
	Oct. 16, 1912	54.7	50.2	6.5	6.0	8.18	8.12	40.2
	Nov. 1, 1912	95.7	81.6	12.2	11.0	5.87	5.81	37.45
M. V.	Oct. 8, 1912	163.0	157.9	12.3	12.2	8.00	8.13	40.5
	Nov. 5, 1912	81.8	90.8	7.3	8.2	5.91	5.87	37.95
F. S.	Oct. 2, 1912	94.7	90.2	7.3	7.1	4.97	5.13	37.9
F. D.	Oct. 1, 1912	56.8	49.1	4.1	4.3	5.12	5.19	37.2

(gramme) calories per gramme of blood are given off to the calorimeters; whereas the corresponding number for a normal person is always below six for the average of the two feet. The difference does not depend upon variations in the calorimeter temperatures in the different experiments. It is essential to point this out, as it is obvious that it is inherent in the method that the lower the calorimeter temperature the greater must be the heat loss per gramme of blood passing through the part. The slight differences in the heat given off by the two hands or by the two feet in one and the same experiment depend upon differences in the calorimeter temperatures.

If the cutaneous vasoconstriction is in the interests of an increase in the blood flow to the organs on which the stress of the infection falls, it is plain that if the increased temperature is to be combated by direct measures the most rational procedure is to hasten the loss of heat without dilatation of the skin vessels, or still better while their constriction is even increased. This indication is admirably met by the cold bath treatment. On the other hand, the use of antipyretics which act by causing cutaneous vasodilatation would seem to be unphysiological, since in diminishing the temperature they cause the withdrawal of blood from the seats of infection.

M. V. was examined for the first time on the day following his admission to the hospital. His rectal temperature was 40.5° C. (104.9° F.), although he had had a full bath two hours before the examination. The flow was only 1.54 grammes per 100 cubic centimeters of foot per minute for the right foot, and 1.50 grammes for the left, with room temperature 22.2° C. On account of hemorrhage nine days after the first examination, it was not considered justifiable to carry out the original program, since, although the examination caused apparently very little disturbance to the patient, absolute rest was obviously enjoined in his case. Accordingly an interval of exactly four weeks elapsed between the first and the second examination of the blood flow. His rectal temperature at the second examination was 37.95° C. (100.3° F.). The foot flow was somewhat smaller than at the first examination (1.24 grammes per 100 cubic centimeters per minute for the right, and 1.40 grames for the left, with room temperature 22.9°). Of course the amount of heat given off per minute to the calorimeter was much greater at the first examination than at the second on account of the higher blood temperature. This renders it necessary to state that it has not hitherto been feasible to determine by actual experiment in a fever case the relation between the rectal temperature and the temperature of the arterial blood at the ankle under the average conditions of our blood flow observations. It has been assumed in the calculations that the difference is 0.6° C., the same as for a normal person. It is, of course, possible that in fever the temperature of the blood as it passes from the heart to the wrist or ankle falls more than in health, since the excess of temperature of the skin over that of the surroundings is greater. Yet the arterial blood moves so rapidly and the large arteries are so well protected that it can scarcely be supposed that any considerable difference exists. It must be taken into account also that in the observations the limbs were covered as far as possible down to the calorimeters. It may therefore be confidently assumed that the calculations are not vitiated in any important degree by the want of direct experimental control of this factor.

The greatest number of observations were obtained on J. B. The first examination of J. B. was made on October 2, 1912, ten days after his admission, more than four weeks from the beginning of his illness, and a week after the maximum temperature (105.8° F.) had been reached. The rectal temperature after the examination was 39.35° C. (102.83° F.). The flow in the feet was the largest observed in this series of fever cases and the only flow which fell within the normal range (viz.: 3.36 grammes per 100 cubic centimeters per minute for the right foot, and 3.82 grammes for the left, with room temperature 24.4° C.).

Six days later, his temperature having meanwhile mounted again and continued high, the foot flow was found to be much smaller and eight days later, on October 16, the rectal temperature being now 40.2° C. (104.36° F.), the flow was only 0.80 gramme for the right foot and 0.74 gramme for the left. The clinical records show great variations in temperature since the first examination and he continued to present disturbing cardiac and other symptoms.

The last examination was made on November 1, 1912, almost seven weeks after admission to the hospital and ten weeks after the beginning of the illness, his temperature being now for the first time fairly stable and at a normal level. The flow was 2.08 grammes per 100 cubic centimeters per minute for the right foot and 1.89 grammes for the left. In view of the fact that the room temperature was more than 2° C. lower on this than on the first occasion, the results indicate that at the first examination the conditions that determine the rate of flow in the feet were more similar to the conditions at the last examination than to those at the two intermediate examinations, in spite of the great difference of body temperature. The most natural explanation is that both at the first and the last examination in this rather protracted case the intoxication was subsiding and the cutaneous vasoconstriction was disappearing. After the first examination, however, a relapse seems to have occurred, the patient's progress being interrupted by complicating incidents (continued ulceration, etc.), the cutaneous vasoconstriction increased, and the temperature ran up again almost, if not quite, to the maximum reached before. In the absence of simultaneous measurements of the hand flow it is impossible to know whether intoxication of the heart contributed to the smallness of the foot flows in the intermediate period, although from the heart symptoms this seems probable. The progressive diminution in the volume of the feet in the first three examinations is a point which may be noted, since it affords a quantitative expression (for a particular part) of the increasing emaciation which was very evident in the body as a whole. The foot volume at the fourth examination is not comparable with the others, as the reduced calorimeters were then used for the first time.

In F. B., a case of pneumonia, the flow at the first examination, on the day of his admission to the hospital and a fortnight from the beginning of his illness, was 2.07

grammes per 100 cubic centimeters of foot per minute for the right foot, and 2.30 grammes for the left, with room temperature 23.0° C.,—flows not perhaps markedly deficient for his age, but certainly not above the normal. Six days later the flow was less (1.36 grammes for the right, and 1.12 grammes for the left foot) with a slightly lower room temperature, but practically the same rectal temperature. Here again in the absence of observations on the hands it cannot be stated what share the weakening of the heart might have had in the diminution of the flow. That it was weakening at this time is probable, as he died four and a half days later, apparently from a general intoxication.

CONCLUSIONS OF SECTION V

1. In the cases of fever investigated the flow in the feet never exceeded the normal flow and was usually much below the normal.

2. In explanation of the relatively small foot flow in the fever cases it is suggested that the vasoconstrictor mechanism of the peripheral parts, especially of the skin, is abnormally excited, and some direct evidence that this is the case is brought forward.

3. The significance of this hypersensitiveness, or at least increased action, of the cutaneous vasoconstrictor mechanism is assumed to be that the peripheral vasoconstriction is a compensatory arrangement which secures for the organs mainly suffering from the infective process an increased flow of blood.

4. On this hypothesis the rise of temperature is, chiefly at least, secondary, inevitably following the vasoconstriction, provided that the metabolism is, upon the whole, not diminished.

5. Accordingly the rational treatment of hyperpyrexia, or of pyrexia if it is considered necessary to treat it, is to abstract heat by a process which will not diminish and may even increase the cutaneous vasoconstriction. This condition is exactly fulfilled by the cold bath, at least as regards its initial effect. Other so-called tonic effects of the cold bath are not considered here.

Antipyretic drugs which act by dilating the cutaneous vessels would seem to be inferior in this regard. They diminish the temperature, it is true, but at the cost of defeating the beneficial redistribution of the blood which it is the function of the peripheral vasoconstriction to insure.

6. It is obvious that for the elimination of a given quantity of heat from the skin by radiation and conduction [4] in fever, a smaller cutaneous blood flow will suffice than with normal body temperature, since the elimination of heat per gramme of blood passing through the surface must be greater in fever owing to the greater difference of temperature between the surface of the body and its surroundings.

I am much indebted to the staff of the City Hospital for their coöperation which has rendered this investigation possible.

As the paper is already unduly long only general summaries of the results in the remaining sections will be given without reference to details of the separate measurements.

SECTION VI. DISEASES OF THE HEART

A few words are necessary in regard to the classification of the cases dealt with in this section. Some overlapping between the groups is unavoidable and the attempt has been made to assign each case presenting a complication of lesions to the group in which the factor seemingly predominant in the clinical picture in so far as light can be thrown upon this by the blood flow measurements would place it. For example, in the group of myocardial affections, cases are necessarily included in which there were very definite and demonstrable valvular lesions, *e.g.*, three cases of mitral stenosis (and insufficiency) in which there was evidence that auricular fibrillation was also present, and that probably this condition with the consequent marked disturbance of the action of the ventricle was, at the time of the investigation at least, a more important factor in the clinical situation than the valvular lesion or at least a factor which differentiated the cases from others with the valvular lesion alone, and lent to them an added gravity.

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[4] Loss of heat by sweat is not considered, since the parts investigated could not lose heat in this way under the conditions of the observations.

In comparing the flows in the whole series of cases investigated with those in normal persons, one is struck by the fact that while in persons suffering from well characterized pathological changes (compensated valvular lesions, for example) the flow may be of the normal magnitude having regard to the age of the patient, the room temperature, and similar conditions, in a larger number of cases it is below the normal, often greatly below it. Sometimes there is good evidence that this diminution in the hand or foot flow is the expression of an increased excitability of the vasoconstrictor mechanism as a whole or at least of the portion of it which presides over the cutaneous vessels not necessarily related to any material diminution in the driving power or the output of the heart. In other cases there is evidence that the diminished flow in the hand (or foot) is in the main the expression of diminished functional capacity on the part of the heart, and associated either with engorgement of the veins and the right side of the heart or with diminution in the filling of the arteries without increased venous pressure.

The question, under what condition the flow in the hands or feet is an indication of the functional capacity of the heart, may be answered provisionally here. Where the hand (and foot) flow is not less than normal it is only in quite exceptional conditions (local vasomotor paralysis of hands and feet?) that any error will be made in assuming that the heart is discharging an amount of blood not inferior to the normal. When, however, the flow in the extremities is permanently and decidedly less than normal several points have to be considered. In many of these cases where the normal ratio of the hand to the foot flow is preserved (see Paper VII of the series, Journal of Experimental Medicine, 1913, xviii, p. 354), in spite of the diminution in the flow and where no anæmia is present, there is often reason to believe that the lessened driving power of the heart is primarily responsible for the diminished flow. On the other hand, in the anæmias (Paper VI of the series, Journal of

Experimental Medicine, 1913, xviii, No. 2) the diminution of the flow in the hand and in the skin generally seems to be a compensating mechanism which permits an even increased quantity of blood to be sent by the heart through the lungs.

SUMMARY

1. The smallest flows observed in the series of cases dealt with in this section have been associated with marked irregularity of the heart, indicating involvement of the mechanism of the heart beat. In some of these cases the cardiac irregularity was associated with valvular lesions, but in those with the very smallest hand flows there was no evidence that the valves were involved.

2. Three cases were diagnosed as auricular fibrillation, all associated with mitral stenosis and insufficiency. While the flow in all was below the normal it was decidedly greater in one patient than in the other two, in spite of his being much the oldest of the three. This corresponded well with his clinical condition, which was good at the time of the examination. The ventricle in spite of its extremely irregular action was upon the whole beating fairly strongly, and was obviously delivering a fair amount of blood to the periphery. On the other hand the patient with the smallest hand flow complained that she was always cold.

3. In a case of mitral stenosis and insufficiency and tricuspid insufficiency in which the heart showed marked arrhythmia in part associated with the respiration, the hand flow was also much below the normal sinus arrhythmia.

4. Abnormally small flows have also been seen in a number of cases diagnosed as myocarditis with regular action of the heart, but feeble heart sounds not accompanied by murmurs.

5. In a certain number of cases diagnosed as myocarditis without valvular lesion in which a serious clinical condition had previously existed, very fair hand flows, not much inferior to the normal, were found when the clinical condition had markedly improved.

6. In several cases of mitral insufficiency with good com-

pensation and no signs of impairment of the myocardium the hand flow was found to be quite up to the normal amount. In one case of mitral stenosis and insufficiency the flow appeared to be even somewhat greater than normal, as if the big, well-compensated heart was discharging even more than the usual quantity of blood.

7. In a case of apparently pure aortic stenosis with seemingly perfect compensation, the hand flow was normal.

8. In two cases of mitral insufficiency with badly broken compensation with venous engorgement, œdema, cyanosis and dyspnœa, the hand flow was much below the normal. In one of these cases a striking diminution occurred a few days before death.

9. In a case of mitral insufficiency with broken compensation, venous engorgement and œdema, but no dyspnœa or cyanosis, the hand flow was quite up to normal. In another case with the same lesions where there was little œdema, no shortness of breath except on exertion and none at the time of examination, the flow was also little if at all inferior to the normal flow, and the restoration of compensation was associated with an actual moderate diminution in the flow.

10. In a case of aortic insufficiency and stenosis, with badly broken compensation (great dyspnœa, pulmonary œdema), the hand flow was greatly diminished. In another case of aortic stenosis and insufficiency with mitral insufficiency, while there were no signs of broken compensation the hand flow was somewhat below the normal.

11. In a case of mitral insufficiency with physical signs of pericardial effusion a flow not much inferior to the normal was found after the patient had been some time in the hospital and had regained compensation and when the heart dulness had decidedly diminished. Two days after leaving the hospital he broke down again and returned with some dyspnœa, cough and swelling of the legs. The hand flow was now found distinctly below its previous value.

While it is obvious that some of the groups of cases are much better represented in the observations than others, as is easily understood from the fact that they had to be collected as chance offered, certain general conclusions which, although of course at present only provisional, are yet entitled to some weight, seem to emerge with sufficient clearness. It is scarcely necessary to say that in some points these conclusions simply confirm what is found by palpation of the radial pulse. But it is by no means the case that even the qualitative result of the blood flow measurement can always be predicted from feeling the pulse.

I. The hand flow is far more apt to be markedly deficient in cases where there is evidence of serious impairment of the myocardium, or more comprehensively and probably more accurately of the mechanisms on which the force and rhythm of the heart's action depend, even when valvular lesions are absent, than in cases where gross valvular lesions exist while the heart's action is strong and orderly. With a heart whose myocardium is seriously crippled, even when the valves are anatomically and probably functionally intact, the hand flow may sink to astonishingly small figures. Nor is this difficult to understand. A pump with somewhat leaky valves may still deliver a good stream when the strokes are strong and regular. No matter how tight the valves are the output will be small if the stroke is feeble, uncertain and irregular. This broad distinction holds even when in cases of valvular disease the clinical signs of loss of compensation are evident. It seems, however, to be less true of aortic insufficiency than of mitral insufficiency. In aortic insufficiency the hand flow appears to be less easily maintained at the normal level and to fall below it more readily when compensation is lost than in mitral insufficiency.

II. Even where there is considerable venous engorgement in cardiac cases the flow in the hands may be little if at all diminished provided that the myocardium is not impaired. A marked diminution in the hand flow in a case of valvular lesion with great engorgement of the veins where the initial hand flow was already distinctly subnormal, appears to indicate failure of the myocardium. On the other hand when in a case of broken compensation the flow in the hand is even above the normal the re-establishment of compensation may be associated with a moderate decline.

III. When in a cardiac case with broken compensation the hand flow is normal or not much diminished the indication is that the myocardium as yet has not suffered serious impairment. A decided diminution in the course of the case may be significant of impending failure of the myocardium.

SECTION VII. CERTAIN VASCULAR CONDITIONS

1. Arteriosclerosis.

It need scarcely be mentioned that several of the cases included in the previous section, in addition to valvular lesions of the heart or myocardial changes, suffered from arteriosclerosis. In this section a few cases were studied in which arteriosclerosis was marked and other lesions, if present, did not dominate the clinical picture. As a general result of the observations it may be stated that in marked arteriosclerosis the flow in the hands is always smaller and the vasomotor reflexes weaker than in normal persons. Vasodilatation is easier to obtain by the application of warmth to the contralateral hand than vasoconstriction by the application of cold.

2. Thoracic aneurism.

For the age of the patients and the temperature of the room the hand flows in the cases of thoracic aneurism examined were either of the normal order of magnitude or at least not so conspicuously deficient as in cases where the stress of the pathological change falls upon the myocardium rather than on the blood-vessels. It is not of course suggested that in some of the cases of aneurism deterioration and disordered function of the myocardium may not be of graver import than the aneurism itself. But in so far as the aneurism, or rather the underlying condition which has occasioned the aneurism, has not led to deterioration of the heart, there is no reason in the mechanics of the circulation why the blood flow through the hand should suffer. This is true even where the form of the pulse wave may be greatly distorted by the presence of the aneurismal sac. For example, in a man 31 years old, suffering from aneurism of the arch of the aorta, very marked differences in the radial pulse on the two sides, differences perfectly evident both to the finger and on the sphygmogram, were associated with equality of the flow between the two hands. The right radial showed a typical pulse of aortic insufficiency with abrupt ascent to a sharp apex and abrupt fall, while the left radial gave a sphygmogram with a rounded apex. The blood pressure in the two brachials was also quite different, the systolic pressure being 157 in the right, and 118 in the left. Three days previously the pressures were 160 (systolic), 45 (change of sound) in the right, and 130, 55 in the left brachial. There was liquid in the left pleural cavity and the physical signs of aortic insufficiency were present.

The blood flow measurement showed an almost absolute equality between the two hands (11.11 grammes per 100 c.c. per minute for the right, and 11.06 grammes for the left with room temperature 23.2°), a perfectly normal flow for a man of this age. The conclusion was drawn that the aneurism in distorting the form of the pulse wave did not interfere with the free passage of blood through the left subclavian artery, and this was confirmed, it is believed, by the necropsy findings. The man died the same night, about 10 hours after the examination, by a rupture of the aneurism into the left bronchus. It is worthy of remark that 10 hours before his death the blood flow in his hands, which no doubt in this case was an index of the output of his heart, was quite normal, although this is of course what was to be expected. He was to die not because his heart was failing but because the wall of the aneurismal sac had been thinned to the bursting point. A very different tale would have been told by the hand flow in a case of impending heart failure.

Of course a sufficient degree of pressure of the sac on a subclavian artery or vein may diminish the flow in the corresponding hand. Yet a distinct unilateral distention of the veins is compatible not only with equality of the flow in the two hands, but even with a preponderance on the side of the distention if other circumstances more than compensate for the increased venous pressure. Thus in a man aged 38 years, with a spherical aneurism of the innominate (as shown by necropsy), with venous obstruction on the right side, there was a decided deficiency in the flow of the left hand as compared with the right (10.91 grammes per 100 c.c. per minute for the right, 8.15 grammes for the left, a ratio of 1.33 : 1). For the room temperature of 28° C., 10.9 grammes is not a large flow, but neither is it decidedly small. The vasomotor reflexes from the right to the left hand were normal in direction, and not strikingly deficient in intensity, showing that the chief afferent paths in the vasomotor reaction to warmth or cold (the nerves of warmth and cold sensation) have not appreciably suffered by stagnation of the circulation due to the pressure of the aneurism on the subclavian vein. Now when pressure is maintained on the arm at a level somewhat below the systolic arterial pressure by means of the cuff of a sphygmometer the warmth sensations suffer early so that it is impossible to appreciate the contact of a warm tube while the sensation of pain is at this stage less affected. As has been pointed out in Paper X of the series (Archives of Internal Medicine, 1913), a certain amount of venous distention, provided that the arterial pressure is correspondingly increased, may even be associated with an increased flow, because of the increased cross-section of the smaller vessels. So far as the arterial path to the right arm is concerned, the conditions would favor a greater flow in the right hand, for as shown at the necropsy the aneurism provides a much wider entrance than normal for the blood going to the right subclavian and possibly a reservoir which helps to maintain the flow during diastole.

3. Miscellaneous vascular conditions, including vascular neuroses.

Among these were three cases of typical Raynaud's disease. In all the flow was small, the diminution being in proportion to the length of time for which the condition had existed. In the earlier cases the contralateral vasomotor reaction to cold was peculiarly intense. In the case of longest standing (8 years) which had gone on to gangrene this reaction was missed probably because of permanent anatomical changes in the vessels and their nerves. In all three cases some general enfeeblement of the circulation seemed to be the background on which the local condition projected itself, since improvement in the general condition, in the earlier stages at least, appeared to be followed by diminution in the frequency and severity of the local attacks.

In a case of dead fingers in an elderly man affecting only the right hand the flows were among the smallest observed in the whole investigation and this not only in the hand obviously affected but also in the other. A fair reflex vasodilatation was obtained in the right hand on the immersion of the left in warm water. The dead condition of the right hand is therefore probably not due to anatomical change in the vessels but to a vasoconstriction.

In a case of diabetic gangrene of the feet more advanced in the left than in the right in a man 63 years old, the flow with a room temperature of 25.6° C. was 1.39 grammes for the right foot and 1.83 grammes for the left, or, allowing for the swelling of the latter, 1.95 grammes. The hand flow was 2.65 grammes for the right hand and 3.32 grammes for the left per 100 c.c. per minute with room temperature 22.0° C. The fact that the flow both in the hands and feet is decidedly below the normal agrees with the well-known feebleness of the cutaneous circulation in diabetes and is probably in part due to cardiac changes, since the ratio of foot to hand flow lies within the normal range. The vasomotor reflex when warm water is applied to the contralateral hand is very poor. Whether this indicates the beginning of pathological changes in the hand arteries also cannot of course be definitely stated. It is in any case interesting to correlate the enfeeblement of this vasomotor reflex with the enfeeblement or disappearance of skeletal reflexes such as the knee jerk, which is known to occur in long-standing cases.

In a case of gangrene of the toes of the left foot of doubtful etiology the flow was 2.15 grammes per 100 c.c. per minute in the right foot and in the left foot 3.42 grammes.

The question whether the gangrene was going to spread was what chiefly interested the physician in charge of the case. The fact that the flow in the feet was so good was interpreted as favorable for the prognosis, although of course it was impossible to say to what extent the flow in the toes themselves had been interfered with. The left foot was somewhat swollen, as shown by the volume measurement. Yet it was only a little over 3 per cent. larger than the right. The greater flow in the left was probably associated with a certain degree of inflammatory reaction. The foot soon healed to a considerable extent.

It was afterward ascertained that the man had frozen his feet the previous winter. The local condition, however, was associated with myocarditis and general cyanosis, the hand flow was extremely small, and the patient eventually died.

The last case to be mentioned in this section is that of a man with local œdema and cyanosis of the right foot and leg which comes on with great rapidity in the standing position and rapidly disappears when he lies down. There was anæsthesia in the affected region and the distribution of the anæsthesia and the history of the case seemed to indicate that a nerve injury was the starting point of the vascular condition. The flow in the right foot was 0.51 gramme per 100 c.c. per minute and in the left 1.35 grammes with room temperature 23.0° C. The flow in the right hand was 3.43 grammes, and in the left hand 3.71 grammes per 100 c.c. per minute with room temperature 22.6° C. While, then, the flow in the hands is much below the normal, which corresponds well with the rather feeble action of the heart and with his anæmic condition, the flow in the left foot preserves a ratio to that in the hands not far from normal. The flow in the right foot, however, is distinctly poor, even in proportion to the poor hand flow. The cause accordingly of the small flow in the right foot is not a central one, but is local. This agrees well with his observation that he cannot keep the right foot warm and that the red color which it first exhibits when he stands soon becomes pale blue. The blood flow measurement corroborates the conclusion that in the right foot the blood is stagnating in the capillaries of the engorged area.

SECTION VIII. DISEASES OF THE NERVOUS SYSTEM

In several cases of early peripheral neuritis confined to one upper extremity it was observed that the flow was distinctly greater on the affected than on the sound side. Thus in a brick-layer, aged 45 years, the flow on the affected (right) side was 10.29 grammes, and only 7.66 grammes per 100 c.c. per minute in the normal hand. The preponderance for the right hand is much greater than the slight excess which is usually found in right-handed individuals. The most plausible explanation is that the vasoconstrictor fibres of the hand are involved in the pathological process and are partially paralyzed. The vasomotor reaction in the affected hand to the immersion of the sound hand in cold water is prompt and strong (the flow being diminished from 10.29 grammes to 5.18 grammes), but it does not last long, and the flow soon increases (to 8.16 grammes) while the sound hand is still in the cold water.

In a case of long-standing right brachial neuritis with marked atrophy of muscles and practical disuse of the hand, the flow was found much less in the affected than in the sound hand (3.98 grammes as against 5.70 grammes). In an unusual case of post-typhoidal neuritis of many years' standing, R. E., the hand which was functionally most affected had the smaller flow (Table V, pp. 144, 145). It was shown in this case and also in a case of traumatic injury to the median nerve (Table VI, pp. 146, 147) in a normal man, O. C. W., that vasomotor reflexes can be elicited by warmth and cold from regions devoid of temperature sensibility, although they are feebler than the normal reflexes. In a case of hemiplegia (cerebral hemorrhage) of nine years' standing the difference was in the same direction, the flow being 4.67 grammes in the paralyzed and 9.15 grammes in the normal hand. Absolutely no vasomotor reaction could be elicited in this case in the paralyzed hand when the sound hand was placed either in cold or warm water. The secondary changes in the blood-vessels of the paralyzed hand and in the vasomotor endings may be supposed to constitute an effective organic block to the reflex vasomotor impulses.

In none of the cases of hemiplegia examined did the flow on the paralyzed side preponderate, while in all the cases of unilateral peripheral neuritis such preponderance existed, except in those of long standing associated with marked muscular atrophy. In tabes the flow, both in hands and feet, was found diminished and the vasomotor reflexes feeble in such cases as were examined.

In a young man recovering from tetanus after treatment with antitoxin the vasomotor reflexes were notably intense. It is unknown whether the excitability of these as well as the skeletal reflex arcs is increased by the toxin. Intense vasomotor reflexes were also observed in a case of cerebral tumor with the signs of increased intracranial pressure. It might be suggested that this was connected with an increase in the excitability of the vasomotor centre in response to the increased intracranial pressure in the interests of the blood flow through the brain.

In two cases of lead poisoning (without palsy) the tendency to reflex vasoconstriction was decided. This was also observed in several cases of alcoholic neuritis. In a case of alcoholic intoxication and in a case of excessive cigarette smoking the opposite was observed, namely, a tendency to marked reflex vasodilatation.

SECTION IX. DISEASES OF THE RESPIRATORY SYSTEM

From the relations of the lungs and pleura to the subclavian vessels it seemed possible that pulmonary lesions, especially unilateral, might produce a demonstrable inequality in the flow in the two hands. The possibility even exists that lesions of the lungs might affect the vasomotor fibres for the upper extremity on their course from the cord through the lymphatic chain, and an effect of this kind entirely or mainly unilateral might be revealed by inequality in the hand flows. Accordingly a series of chronic cases of pulmonary tuberculosis affecting chiefly one lung were examined. While no difference in the

TABLE V.

SUMMARY OF RESULTS ON R. E. (See p. 142.)

Date.	Temperature C. of				Vol. of hand in c.c.		Heat given off in small calories.			Blood flow gms. per min.		Flow per 100 c.c. of hand per min.		Notes.
	Room.	R. Cal.	L. Cal.	Art. Bld.	Right.	Left.	Right.	Left.	In mins.	Right.	Left.	Right.	Left.	
April 26	24.0	30.82	30.69	36.6	379	397	951	1,469	15	12.19	18.41	3.21	4.56	For the 15 mins. preceding the vasomotor test.
	....	30.85	30.78	....	...	...	459	598	6	14.78	19.02	3.90	4.71	For 6 mins. immediately preceding the vasomotor test.
	24.0	....	30.88	....	...	...	....	444	6	....	14.37	....	3.56	First 6 mins. immersion of right hand and wrist in warm water.
	....	....	31.04	....	...	...	....	1,161	8	....	29.00	....	7.19	Next 8 minutes.
	23.6	....	31.18	....	...	...	....	287	3	....	19.61	....	4.86	First 3 mins. with right hand and wrist in cold water.
	....	....	31.22	....	...	...	....	636	12	....	10.94	....	2.71	Next 12 minutes.
May 2	25.4	31.10	31.19	36.6	361	385	541	578	10	10.93	11.87	3.03	3.08	For 10 mins. before vasomotor test.
	25.4	31.14	....	....	...	...	237	....	5	9.64	....	2.67	....	First 5 mins. immersion of left hand in warm water.
	24.9	31.28	....	....	...	...	1,150	....	8	30.02	....	8.31	....	Next 8 minutes.
	25.0	31.44	....	....	...	...	271	....	2	29.18	....	8.08	....	First 2 mins. with left hand in cold water.
	....	31.55	....	....	...	...	423	....	6	15.51	....	4.29	....	Next 6 minutes.
May 8	22.9	31.04	31.06	36.95	403	421	1,213	1,407	12	19.00	22.12	4.71	5.25	For the 12 mins. preceding vasomotor test.
	22.9	....	31.27	....	...	...	....	867	10	....	16.96	....	4.03	First 10 mins. with only anæsthetic part of right hand in warm water.
	22.8	....	31.41	....	...	...	....	1,012	10	....	20.29	....	4.82	Next 10 minutes.
	22.8	....	31.52	....	...	...	....	329	4	....	16.83	....	4.00	First 4 mins. immersion of right wrist also in warm water.
	22.8	....	31.63	....	...	...	....	1,009	8	....	26.33	....	6.25	Next 8 minutes.
	22.7	....	31.78	....	...	...	....	686	8	....	18.42	....	4.37	First 8 mins. immersion of anæsthetic part only of right hand in cold water.

TABLE V.—*Continued.*

Summary of Results on R. E.

Date.	Temperature C. of				Vol. of hand in c.c.		Heat given off in small calories.			Blood flow gms. per min.		Flow per 100 c.c. of hand per min.		Notes.
	Room.	R. Cal.	L. Cal.	Art. Bld.	Right.	Left.	Right.	Left.	In mins.	Right.	Left.	Right.	Left.	
May 8	22.7	....	31.83	....	...	...	....	282	5	....	12.24	....	2.90	Next 5 minutes.
	22.8	....	31.85	....	...	...	....	460	9	....	11.13	....	2.64	For 9 mins. immersion of right hand and wrist in warm water.
May 18	24.8	30.98	30.97	36.55	391	409	1,158	1,317	18	12.83	14.57	3.28	3.56	For 18 mins. preceding the vasomotor tests.
	24.8	31.02	31.02	....	...	...	630	719	10	12.66	14.44	3.24	3.53	For the last 10 mins. of this period.
	24.6	....	31.11	....	...	...	....	383	6	....	13.04	....	3.19	First 6 mins. immersion of anæsthetic part of right hand in cold water.
	24.6	....	31.19	....	...	...	....	524	6	....	18.10	....	4.42	Next 6 minutes.
	24.9	....	31.35	....	...	...	....	1,146	13	....	18.83	....	4.60	For 13 mins. during immersion of anæsthetic part of right hand in warm water.
	24.8	....	31.52	....	...	...	....	650	8	....	17.94	....	4.38	For 8 mins. immersion of anæsthetic part of right hand in cold water.
	24.7	....	31.61	....	...	...	....	616	12	....	11.54	....	2.82	For 12 mins. immersion right hand and wrist in cold water.
	24.9	....	31.67	....	...	...	....	410	5	....	18.67	....	4.56	For the first 5 mins. immersion of right hand and wrist in warm water.
	24.9	....	31.73	....	...	...	....	308	6	....	11.83	....	2.89	For the next 6 mins. of immersion in the warm water.
	24.9	....	31.79	....	...	...	....	598	8	....	17.44	....	4.26	For 8 mins. with right hand dried and wrapped up.

TABLE VI.

SUMMARY OF BLOOD FLOW OBSERVATIONS ON O. C. W. (See p. 162)

Date.	Temperature C. of calorimeter.				Vol. of hands, c.c.		Heat given off (small cals.).			Flow in hands per min.		Flow per 100 c.c. per min.		Notes.
	Room.	Right.	Left.	Art. Blood.	Right.	Left.	Right.	Left.	In mins.	Right.	Left.	Right.	Left.	
Oct. 15	22.6	31.32	31.35	36.65	447	436	2,537	2,273	16	33.05	29.78	7.39	6.83	Before vasomotor reflex tests.
	22.8	31.61	....	....	...	...	155	....	2	17.08	....	3.82	....	Anæsthetic phals. in cold water (first 2 mins.).
	22.9	31.72	....	....	...	...	1,053	....	7	33.90	....	7.58	....	Anæsthetic phals. in cold water (next 7 mins.).
	23.0	31.87	....	....	...	...	431	....	3	33.39	....	7.24	....	Anæsthetic phals. in warm water (first 3 mins.).
	23.1	32.04	....	....	...	...	1,157	....	5	55.77	....	12.47	....	Anæsthetic phals. in warm water (next 5 mins.).
	32.2	32.23	....	....	...	...	638	....	4	40.09	....	8.96	....	Whole left hand in warm water (first 4 mins.).
	23.2	32.39	....	....	...	...	915	....	4	59.66	....	13.34	....	Whole left hand in warm water (next 4 mins.).
	23.3	32.55	....	....	...	...	956	....	8	32.38	....	7.24	....	Whole left hand in cold water.
Dec. 19	23.3	31.17	31.17	36.55	431	407	2,219	2,018	10	45.82	41.67	10.63	10.23	Before vasomotor reflex tested.
	23.3	31.46	....	....	...	...	206	....	2	22.48	....	5.21	....	Anæsthetic phals. in cold water (first 2 mins.).
	23.3	31.64	....	....	...	...	1,394	....	8	39.43	....	9.15	....	Anæsthetic phals. in cold water (next 8 mins.).
	23.3	31.87	....	....	...	...	567	....	4	33.65	....	7.80	....	Anæsthetic phals. in warm water (first 4 mins.).
	23.35	32.06	....	....	...	...	1,153	....	7	40.76	....	9.45	....	Anæsthetic phals. in warm water (next 7 mins.).
	23.3	32.25	....	....	...	...	464	....	3	39.96	....	9.27	....	Whole left hand in warm water (first 3 mins.).
	23.3	32.50	....	....	...	...	1,669	....	8	57.23	....	13.27	....	Whole left hand in warm water (next 8 mins.).
	23.2	32.81	....	....	...	...	1,032	....	9	34.06	....	7.90	....	Whole left hand in warm water (first 3 mins.).
	23.25	33.01	....	....	...	...	1,032	....	8	40.49	....	9.39	....	Whole left hand dried and wrapped up.

TABLE VI.—*Continued.*

SUMMARY OF BLOOD FLOW OBSERVATIONS ON O. C. W.

Date.	Temperature C. of calorimeters.				Vol. of hands, c.c.		Heat given off (small cals.).			Flow in hands per min.		Flow per 100 c.c. per min.		Notes.
	Room.	Right.	Left.	Art. Blood.	Right.	Left.	Right.	Left.	In mins.	Right.	Left.	Right.	Left.	
Dec. 21	22.9	30.82	....	36.50	431	...	2,012	....	9	43.73	....	10.14	....	Before vasomotor tests.
	22.9	31.10	....	....	...	...	242	....	2	24.89	....	5.77	....	Anæsthetic phals. in cold water (first 2 mins.).
	22.9	31.33	....	....	...	...	1,684	....	8	45.26	....	10.50	....	Anæsthetic phals. in cold water (next 8 mins.).
	22.6	31.58	....	....	...	...	416	....	3	31.31	....	7.28	....	Anæsthetic phals. in warm water (first 3 mins.).
	22.5	31.79	....	....	...	...	1,448	....	7	48.79	....	11.32	....	Anæsthetic phals. in warm water (next 7 mins.).
	22.7	31.99	....	....	...	...	263	....	2	32.39	....	7.51	....	7 phals. left hand in warm water (1st 2 mins.).
	22.95	32.23	....	....	...	...	1,782	....	10	46.37	....	10.75	....	7 phals. left hand in warm water (next 10 mins.).
	23.25	32.54	....	....	...	...	1,110	....	9	34.60	....	8.02	....	7 phals. of left hand in cold water.
	23.35	32.70	....	....	...	...	440	....	3	43.27	....	10.04	....	Whole left hand in cold water.
	23.25	32.98	....	....	...	...	1,160	....	6	61.02	....	14.15	....	Whole left hand in warm water (next 6 mins.).

hand flows was established which could be connected with the unilateral character of the pulmonary lesion, a fact which at first sight seemed very puzzling, came out, namely, that the hand flow was in general large in these chronic cases with extensive fibroid change, whereas in early pulmonary tuberculosis it was apt to be small. This difference as well as the unusual stability of the large hand flow in some of the chronic cases against changes of external temperature suggested that the anatomical changes in the vascular path through the lungs are a factor. If the total vascular path in the lungs is narrowed the output of the heart per minute can still remain normal if the average linear velocity of the blood in the still functioning parts of the pulmonary circuit is correspondingly increased. This would not require the return of a greater volume of blood per unit of time to the right side of the heart and therefore would not entail a diminution in the quantity of blood circulating in the peripheral parts (see Section on the Anæmias, p. 113). Nor would it necessarily entail any increase in the rate of the heart. If then the heart rate is substantially increased, as in all these cases, the normal flow through the diminished lung area may be maintained while an amount of blood even greater than the normal passes through the hands. The better filling of the peripheral paths might conceivably even act as a safety-valve against overfilling of the diminished and now unaccommodating pulmonary path.

In early tuberculosis, on the other hand, the vascular capacity of the lungs is not diminished. On the contrary, it is to be supposed that more blood than normal will be supplied to the infected area to combat the infection, and that this increase in the amount of blood going to the lungs may be obtained by vasoconstriction in parts like the hands. This suggestion is put forward with diffidence and in an entirely provisional way in the attempt to harmonize the results obtained on the two groups of cases, and further observations may show its futility.

A large number of cases of unilateral pleural effusion were examined from the same standpoint. In the great majority of these a deficiency in the hand flow on the side of the effusion was found. But that this is not associated with the more mechanical effect of the fluid in the sac seems to be indicated by the fact that on removal of the liquid the difference is not, as a rule, abolished. There is some reason for thinking that it is the anatomical change in the pleura itself, the extension, for instance, of the tubercular process to the pleura from the lung, and not the presence of fluid as such in the sac, which is the factor really associated with the change in the hand flow. It must be remembered that the hand flow measurements are made with the patient in the sitting posture, so that fluid in the pleural sac will not in general occupy the part of the sac in relation with the subclavian vessels. For some time after the withdrawal of the fluid the hand flow is apt to be decidedly diminished on both sides, possibly because the expansion of the previously compressed lung entails the provision of a large total volume of blood for the pulmonary circuit.[5]

In pulmonary emphysema the hand flow also tends to be large. The same explanation might be offered as in the cases of advanced tuberculosis.

SECTION X. MISCELLANEOUS CASES

A considerable number of cases not coming under any of the above headings were studied. The only one which will be mentioned here, on account of the exigencies of space, is a case of Graves's disease. The flow in the hands was exceptionally large, a fact quite in agreement with the flushed surface, the subjective feeling of warmth and the rapid and strong pulse. Immersion of the left hand in cold water (which was very disagreeable to the patient) caused a reduction of the flow in the right hand from 14.18 grammes to 7.82 grammes per 100 c.c. per minute, and the reduction persisted during the period of immersion (5½ minutes).

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[5] The work on the cases with fluid in the pleural cavities was done in collaboration with Dr. Bucher of the Cleveland City Hospital resident staff.

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OBSERVATIONS ON TETANY IN DOGS.

RELATION OF THE PARATHYROIDS TO THE THYROID; RELATION OF TETANY TO AGE, AMOUNT OF PARATHYROID TISSUE REMOVED, ACCESSORY PARATHYROIDS, PREGNANCY, LACTATION, RICKETS, SULPHUR, AND DIET; RELATION OF PARATHYROIDS TO SUGAR TOLERANCE; EFFECT OF CALCIUM SALTS.*

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THE DISTRIBUTION OF PARATHYROID TISSUE AND THE RELATION OF THE PARATHYROIDS TO THE THYROID.

As a complicating factor in thyroid work during the past eight years I have observed thirty-eight cases of tetany and three instances where total removal of the thyroid lobes was not followed by any of the phenomena of tetany.

The frequency of tetany following thyroidectomy in dogs is an index to the constancy of location of the parathyroid glands. On account of the fact that in most of these cases partial thyroparathyroidectomy was done from time to time extending over months and sometimes years before the insufficiency became clinically detectable, ample opportunity was offered for compensatory adjustment, and in this way some cases escaped that would otherwise have had at least a transient tetany if the same amount of parathyroid tissue had been removed suddenly.

In all carnivora it is exceedingly difficult to remove totally even the normal thyroid without obtaining at least a transient tetany on account of the intimate anatomical relation of the parathyroids to the thyroid, while in man and the herbivora this difficulty rarely arises on account of the wide separation of the inferior or external or IIId parathyroids from the thyroid lobes. In dogs the difficulty is of course greatly increased when the thyroid lobes are enlarged, as they are in about 90 per cent. in this locality. There is much writ-

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ten concerning the distribution of the parathyroid tissue. Its origin from four separate anlagen enhances the possibilities for abnormal distribution outside the thyroid area. In dogs aberrant parathyroids are most frequently found in connection with the thymus. In one series of routine examinations of ninety-eight thymuses, I accidentally included parathyroids in the specimens for histological examinations on two occasions and in a case of transient tetany following removal of both lobes of the thyroid I found at post-mortem examination 257 days later a large accessory parathyroid in the thymus. In the three instances (A–106, A–123, and A–194) where following complete removal of both lobes not even transient tetany developed, no parathyroid tissue was found at the routine post-mortem examination, though several suspected bits of tissue were examined histologically.

Parathyroid tissue unconnected with the thyroid lobes in sufficient amounts to maintain life after the removal of both thyroid lobes is present in at least 5 to 6 per cent. of dogs. This percentage is further increased (1) by partial parathyroidectomy extending over months and years which allows of the development of any compensatory mechanism, and (2) by the temporary use of calcium salts which will occasionally tide the animal over an otherwise fatal tetany.

These facts concerning the distribution of parathyroid tissue, and the influence of compensatory hypertrophy and calcium salts are of importance in the controversy that has arisen as to the relation of the parathyroids to the thyroid and their importance to life.

Bearing on the question of the interrelationship of the parathyroids and thyroid which some English observers, notably Vincent (1) and Forsyth (2), have supported are the only two cases of operative myxedema in dogs we have observed (both transient), and in both of these transient and partial tetany not associated with the myxedema developed. The cases are given below.

Dog A–112.—Female fox terrier. Jan. 11, 1908. Weight 5.5 kilos. Jan. 15. Entire left lobe and two thirds of right lobe (weight 4.15 gm.) removed. Mar. 15. Two pups born. Mar. 25. Removed about one half of remaining portion of right lobe. Mar. 26. Violent tetany. Calcium chloride and milk given daily until Apr. 6. Oct. 29. Five pups born. Nov. 3. Violent tetany. Milk and calcium chloride given for three days; tetany cleared up. Dec. 3. Pups weaned. Dec. 7–18. The remainder of the right lobe (weight 0.25 gm.) was removed, and 10 c.c. of saturated aqueous solution of calcium chloride were given daily. Dec. 24. Hair falling out, skin dry and itchy. Weight 5.9 kilos. At first it was thought to be mange and the dog was given sulphur rubs, but during January, 1909, alopecia became very marked and the dry skin was everywhere visible. Jan. 29. Weight 7.2 kilos. Feb. 12. Weight 7 kilos. New coat of hair is beginning to come in. Feb. 26. Weight 6.2 kilos. Mar. 15. Weight 6.1 kilos. New coat of hair about 0.5 cm. long. In heat. May 24. Two pups born. June 5. Weight 5.7 kilos. July 10. Weight 6 kilos. Aug. 10. Weight 6.2 kilos. Sept. 14. Weight 6.2 kilos. Oct. 4. Weight 5.9 kilos. Nov. 26. Weight 5.9 kilos. Dec. 9. Killed in fight with another dog.

Autopsy.—One large accessory parathyroid was found in the thymus, and three small aortic thyroids were in a state of marked hyperplasia.

Dog A–183.—Female mongrel. Nov. 16, 1909. Weight 10 kilos. Nov. 16–23. 1 c.c. of Lugol's solution given. Dec. 1. Bit of left lobe removed. Weight 0.45 gm. Dec. 1, 1909, to Feb. 9, 1910. Dog received 1 gm. of sodium cyanate daily. Dec. 15. Another bit of left lobe was removed. Weight 1.25 gm. Jan. 6, 1910. Remainder of left lobe removed (weight 2.49 gm.). Jan. 19. Bit of right lobe removed (weight 0.67 gm.). Feb. 9. Bit of right lobe removed (weight 1.58 gm.). June 13. Weight 10.2 kilos. Oct. 11. Nine pups born. Nov. 15. Pups weaned. All have strikingly enlarged thyroids. Oct. 15. Weight 12 kilos. Hair falling out. Jan. 6, 1911. Loss of hair is marked. Weight 12.2 kilos. Feb. 12. Weight 11 kilos. New hair coming in. Mar. 3. Weight 10.2 kilos. Apr. 1. Weight 9 kilos. Active; coat glossy. Apr. 11. Remaining portion of right lobe isolated, about size of a medium olive, much hypertrophied. Removed portion (weight 4.6 gm.) leaving a small stump. Apr. 13. Violent tetany. Calcium chloride solution by stomach. Apr. 18. Weight 9.6 gm. Occasional tetany sometimes mild and often severe, always controlled by calcium lactate. May 1. Impregnated. May 20. Pregnant. Suddenly taken with violent tetany; relieved by calcium lactate. Occasional twitchings until June 30, nearing full term, severe tetany, calcium lactate. July 1. Tetany again, calcium lactate. Was in tetany daily until July 6, when she died of tetany shortly after the birth of seven living full term pups.

Histological examination of the remaining stump of the thyroid lobe revealed a trace of parathyroid tissue in the dense scar tissue of the thyroid capsule. The thyroid tissue is in a state of marked hyperplasia. Two aortic thyroids are present, but no other parathyroid tissue is found.

In these two experiments the tetany was dissociated from the myxedema. In dog A–112 the last attack of tetany preceded by about forty days the onset of myxedema which occurred following the last operation for total removal of the thyroid lobes. The myxedema cleared up in three months and the dog remained in apparent health clinically until killed on December 9, thirteen months after the last attack of tetany and nine months after the disappearance of myxedema. In dog A–183 the myxedema developed after the fifth operation of partial removal of thyroid (about nine tenths), and completely cleared up two months before the onset of tetany on the day after the sixth operation for removal of 4.6 grams of the much hypertrophied stump of the right lobe. The dog remained subtetanic with the aid of calcium salts until the end of pregnancy, when an uncontrollable parathyroid insufficiency developed and ended fatally.

Such observations when compared with the experiences of others, —Simpson (3) with tetanies in sheep; Halsted (4), MacCallum (5), Erdheim (6), and others with tetanies in dogs; Kocher (7), Reverdin (8), and Fuhr (9) with total thyroidectomy in man; Maresch (10), Erdheim (11), and Getzowa (12) with congenital defects; and Roussy and Clunet (13) with spontaneous myxedema, —leave no doubt that as regards myxedema and tetany the parathyroids and thyroids are anatomically, physiologically, and pathologically independent structures.

THE RAPIDITY OF THE DEVELOPMENT OF TETANY AND THE RELATION OF TETANY TO AGE, AMOUNT OF PARATHYROID TISSUE REMOVED, ACCESSORY PARATHYROIDS, PREGNANCY, LACTATION, RICKETS, SULPHUR, AND DIET.

I have seen violent tetany develop as early as seven hours after the removal of the parathyroids (dogs A–149 and A–167) and end fatally within eleven hours of the operation. In our series the average time between the last operation and the onset of tetany was eighteen to twenty-four hours. This has impressed me as relatively more rapid than the average time intervals reported by other observers. The conditions are not quite comparable as usually the parathyroidectomy is made at a single operation, while in nearly all of our cases partial thyroparathyroidectomy had been practiced for weeks and months and occasionally a year before the final operation precipitating the tetany. It is therefore possible that the factor of safety or protective reserve was greatly reduced before the final operation.

Several factors influence the rapidity of onset of tetany: (1) age, (2) the amount of parathyroid tissue removed, (3) the presence of inaccessible accessory parathyroid tissue, (4) pregnancy and lactation, (5) rickets, (6) the use of sulphur, and (7) the diet.

Age.—The age of the animal, as many observers have pointed out, is important. Simpson (3) in his work with sheep showed that lambs usually develop tetany following parathyroidectomy, while in yearlings he never observed a fatal tetany, and in old sheep there were no tetanic manifestations at all. In dogs and cats tetany follows the parathyroid removal at any age so that the age factor cannot be shown in this way. The young are, however, more susceptible. The difference due to age is suggested by the following observations. I ligated the superior thyroid arteries on both sides in four pups (A–203, A–204, A–205, and A–206) of the same age (sixty-two days) and same litter, and in all violent tetany developed on the following day, eighteen hours after the ligations. They died of tetany on the eighth, twelfth, ninth, and eighth days, respectively, although calcium lactate was given daily. At autopsy the wounds were healed *per primam.* Only the regions of the superior poles had been traumatized by the operative procedure. The thyroid lobes were somewhat enlarged in each case and in a state of marked hyperplasia. Anemic necrosis roughly involving the upper half of the lobes was present in each case. The inferior thyroid artery, which is normally very small in the dog, was intact and uninjured in all. In twelve similar operations in adult dogs undertaken to study the effect of superior thyroid artery ligation none developed tetany although there was in all a small zone of necrosis at the upper poles involving in some instances a third of the lobe. While the difference in outcome between young pups and adults may be explained principally on the difference in the extent of the necrosis still this can scarcely be the whole explanation. These pups were slightly rachitic and this also is probably an important factor.

Amount of Parathyroid Tissue Removed.—In adult dogs under normal conditions of food and environment one uninjured IIId parathyroid is sufficient to prevent fatal tetany. Many cases are reported where a IVth, or even smaller bit of parathyroid tissue has prevented all signs of tetany. I have seen three cases (dogs A–106, A–123, and A–194) where total removal of the thyroid lobes with their normal quota of parathyroids induced no symptoms. The routine autopsies of these cases failed to reveal any accessory parathyroid tissue although several suspected bits were examined histologically. The examinations were in no sense complete, as such a procedure would involve serial sections of the entire neck and upper thorax, and I am convinced that accessory parathyroids were present somewhere in the parathyroid area. On the other hand, I have seen typical and violent tetany occur in a lactating bitch, where four parathyroids were intact, as ascertained at autopsy.

It is clear from these extremes and from the larger number of cases with intermediate amounts of parathyroid tissue showing variations in the occurrence of tetany that other factors than quantity of parathyroid tissue determine the onset of tetany. Thus when an anatomical insufficiency exists there exists also a physiological insufficiency, but the reverse is often not true since a physiological or relative insufficiency may exist when two and even four parathyroids are intact.

The same is, of course, true of the thyroid tissue,—that where an anatomical deficiency exists a physiological insufficiency exists also, but in the spontaneous thyroid insufficiencies and even in the induced insufficiencies there is usually an excess of thyroid tissue in the early stages.

Pregnancy and Lactation.—These factors tend to induce a relative parathyroid insufficiency. In 1888 Halsted (4) observed this in his cases of partial parathyroidectomy in dogs which developed tetany late in pregnancy. Since then many workers have observed this tendency. There were five cases in this series (dogs A–112, A–113, A–132, A–161, and A–183) where tetany developed with pregnancy or lactation.

In dog A–112 partial thyroparathyroidectomy, followed by a transient tetany for four days, was done six months before the next pregnancy. The dog developed tetany early in lactation which was controlled by calcium salts. The remainder of both lobes was removed later without causing tetany, calcium salts being given for eleven days. Six months later the animal gave birth to another litter of pups without any tetany resulting.

In dog A–183 a mild tetany continued throughout the pregnancy, which was controlled until the last week by the use of calcium salts.

Then in spite of the daily use of calcium lactate the tetany became severe and terminated fatally at the birth of the full term pups. Another bitch (A–113) aborted during a severe tetany that probably could have been prevented by calcium salts.

In another case (A–132) following a first operation for the removal of one and three fourths thyroid lobes on December 7, 1908, a transient tetany developed which was controlled by the administration of calcium salts for ten days. The dog remained free from tetany during the next pregnancy and lactation (May 1 to August 1, 1909) but developed tetany on April 1, 1910, thirteen days before the birth of a second litter of pups. This was wholly controlled by calcium lactate until the birth of the pups, then crushed bone was substituted which probably prevented tetany during lactation. She remained in apparently good health for forty days after weaning the pups and was used for other experiments.

In another case (A–161) violent tetany developed during lactation with at least four parathyroids intact, as was determined later by operation and autopsy. The regular diet of cooked meat with bread but no bone had been used. A synopsis of the protocol follows.

Dog A–161.—Female mongrel; pregnant. Mar. 17, 1909. Thyroid lobes palpable. Sulphur and lard to be given daily (50 gm. of lard containing 5 gm. of powdered sulphur). Weight 9 kilos. Mar. 18. Bit of left lobe, lower pole (weight 0.4 gm.) removed for histological examination. Mar. 21. Stitches removed, wound healed; protective bandage. Mar. 27. Five pups born. Average weight 195 gm. Apr. 2. Weight 7.5 kilos. Stools black and tarry; slight diarrhoea. Apr. 13. Weight 7.2 kilos. Dog is losing weight steadily. This morning a typical and severe tetany developed. At examination the dog is lying on the right side, legs extended, respirations 154. Pulse with stethoscope 224. Marked salivation. Pupils dilated, palpebral fissures also widened. Dilatation of the peripheral vessels. Ears, nose, paws, and skin surface generally hot to the touch. Temperature 104° F. All muscles spastic with fine constant tremors and rapidly recurring coarse jerky twitchings of muscle groups all over the body, in the legs, back, jaws, neck, etc. No obvious gastric dilation. Received one dose of 40 c.c. saturated aqueous solution of calcium chloride by stomach tube, and in twenty minutes she was free from general symptoms of tetany, and able to walk but weak. Sulphur stopped. During the afternoon of the same day another bit of the left lobe, lower pole (weight 1.33 gm.) was removed. The thyroid had enlarged considerably since the last operation. A small IVth parathyroid was attached to the bit of thyroid removed. The dog rallied quickly and ate heartily in the evening. Apr. 14. In excellent condition. Apr. 17. In excellent condition.

Nursing four pups, the other one having been killed at birth as a control. Average weight of the pups is now 755 gm. Apr. 21. Bandage and stitches removed, wound healed, protective bandage. Weight 6.8 kilos. Apr. 22. Started sulphur again, 5 gm. daily. Apr. 29. Definite though mild tetany. Dull but able to stand up, gait ataxic, jaws, legs, back, and head constantly twitching. No tachypnea. Pulse 130. Sulphur stopped but no calcium given or any change in daily routine. Apr. 30. Free from tetany. May 6. Pups weaned. The dog has remained free from any outward signs of tetany, and in the afternoon in attempting operation she choked up with mucus and died in spite of attempts at resuscitation.

Autopsy.—Performed at once. Trachea blocked with mucus. Thyroid lobes enlarged. The remaining part of the left lobe weighs 5.22 gm. The intact right lobe weighs 7.92 gm. The two large external or IIId parathyroids are normally placed. The IVth parathyroid on the right lobe is also prominent. No other parathyroid tissue is found. Thymus large and persistent. Spleen normal. Adrenals, liver, kidneys, and lungs, appear normal. No accessory thyroids could be seen or felt in the aortic area.

Histological Examination.—The specimen of thyroid removed on Mar. 18 showed colloid early hyperplasia; the specimen removed on Apr. 13 showed colloid early hyperplasia; and the specimen removed on May 6 showed colloid moderate hyperplasia.

The parathyroid cells are large and more distinct than normally. There is no evidence of hyperplasia.

Summary.—The bitch developed violent tetany twenty-four days after starting sulphur and seventeen days after the birth of five healthy pups. A single administration of calcium chloride relieved the tetany at once. The sulphur was stopped for nine days following the tetany and then started again. Seven days later the dog developed mild tetany, and on stopping the sulphur no further evidence of tetany developed during the next seven days.

It may be stated, therefore, that in dogs as in man tetanies tend to develop late in pregnancy and occur even more frequently during lactation. The most important question is, Are these pregnancy and lactation tetanies identical fundamentally with those due to parathyroid extirpation? Several authors have answered this question affirmatively. In the cases that I have observed in dogs there are no objective differences to be made out. They present the same clinical manifestations, though usually milder, and they react with calcium salts in the same way.

Since the discovery by MacCallum (14) and Parhon and Ureché (15) of the effect of calcium on parathyroid tetany, it has been suggested that pregnancy and lactation predispose to tetany because at these times the mother suffers an increased depletion of mineral salts among which is calcium. This view draws support from the facts that calcium salts permanently relieve such tetanies, that feeding foods rich in lime salts or giving lime salts during a second pregnancy will prevent tetany in animals that during their earlier pregnancies developed tetany, and that tetany develops very quickly (six to twelve hours) after removing the parathyroids in lactating or recently lactating animals (Carlson (16)).

I am inclined to think that the administration of large amounts of sulphur favors the development of tetany. From a considerable experience with sulphur in relation to thyroid hyperplasia I came to the conclusion that those dogs which had been given sulphur (and most of our tetany cases had had sulphur) for three to four weeks developed tetany earlier, more violently, and possibly in the presence of more intact parathyroid tissue than otherwise. The case cited above (dog A–161), which cleared up so quickly when sulphur was stopped, reappeared after it was started again, and again cleared up after it was stopped, other conditions remaining constant, was further evidence that the administration of sulphur over long periods of time aids to some extent in bringing about a state of nutrition favoring the development of tetany. How it operates is of course mere speculation. Sulphur is not wholly inert. The formation of sulphides in the intestine and the slight laxative effect suggest that possibly some of the alkaline earths are withdrawn from the field of absorption by this element.

Influence of Foods on Tetany.—Meats aggravate the symptoms, and milk, bone, and other foods rich in calcium are protective against tetany or delay its onset. I have seen several instances where bone administration delayed the onset of tetany. No other substance besides calcium has been found to have this effect. Similar effects of an extremely mild and probably more complex nature have been claimed for magnesium and strontium, but in our hands they have yielded negative results. It is certain that tetany is a vastly more complex nutritional disturbance than a calcium deficiency. Of the diseases favoring the development of tetany, rickets stands first. Rachitic pups are more quickly affected by parathyroid removal than normal pups, and tetany is induced following the removal of a smaller amount of parathyroid tissue than in normal pups.[1]

[1] Pups almost invariably become rachitic when fed a diet of bread, liver, lung, and heart muscle, although if crushed bone is added it is prevented. Similar observations have been made with lion cubs at the London Zoölogical Gardens (17).

The close relationship between infantile tetany (carpopedal spasm) and rickets has long been known and many observers believe that this form of tetany is identical with true parathyroid tetany. Yanase (18) reported the finding of hemorrhages in the parathyroids in a significant number of cases of tetany in rachitic infants and believed that a direct relationship existed, but Oppenheimer (19), Bliss (20), Jörgensen (21), and others could not confirm this finding. There could be a grave functional insufficiency without any gross lesions. If the parathyroids were affected we should rather expect an hypertrophy or hyperplasia as a more frequent sign of insufficiency than the presence of atrophic changes, just as occurs in the thyroid. Slight degrees of parathyroid hypertrophy are extremely difficult of proof, as the mammalian parathyroid does not appear capable of a striking overgrowth. Erdheim (22), Bauer (23), and Strada (24) have described hypertrophic changes in the parathyroids in osteomalacia in man. In rickets and infantile tetany it is certain that no marked overgrowth of the parathyroids occurs and calcium does not usually affect this form of tetany. However, that some important connection exists between rickets and infantile tetany and between rickets and the ease and rapidity of onset of true parathyroid tetany in dogs seems established. How much may be due directly to the parathyroids and how much is due to reducing the factors of safety, one of which is certainly calcium, remains unknown.

RELATION OF THE PARATHYROID GLANDS TO SUGAR TOLERANCE.

Dogs are not favorable animals for this work because it is practically impossible to remove the thyroid lobes without destroying the IVth and seriously injuring the IIId parathyroids. Most of the discordant results reported in the literature are attributable to this factor, a notable illustration being Hirsch's (25) observations, when in 1906 as a result of experiments with six thyroidectomized dogs he concluded that the thyroids exercise an important control over carbohydrate metabolism; and two years later, as a result of experiments on fourteen dogs, he concluded that it was not the thyroid but the parathyroid extirpation that produced glycosuria and lowered the sugar tolerance. He found the glycosuria and hyperglycemia parallel.

Underhill and Hilditch (26), in 1909, as a result of experiments of thyroparathyroidectomy and partial thyroparathyroidectomy showed that sugar tolerance was measurably reduced when three parathyroids were removed, but that two intact parathyroids could maintain normal control over sugar tolerance. Our observations confirm the above findings in that they show that it is not the loss of the thyroid but of the parathyroids that so quickly lowers sugar tolerance. Blood sugar estimations were not made on any of the cases.

The plan followed was to obtain the average amount of glucose per kilo of body weight that each dog could take without alimentary glycosuria, and then to repeat the observations after parathyroidectomy. The technical routine was as follows: Urine was withdrawn with a catheter, and glucose solution containing 20 gm. of glucose per 100 c.c. of distilled water, to which 0.2 per cent. hydrochloric acid was added, was given by stomach tube. The dogs were catheterized in one and two hours. All dogs were on the regular house diet, fed once daily in the afternoon, and sugar tolerance estimations were made in the morning, an interval of at least three days, and in most cases more, being allowed between observations. The Worm-Müller, Nylander, and Benedict qualitative tests were used with each specimen.

Ten dogs were thus observed and the results are given in table I.

TABLE I.

Dog No.	Before parathyroidectomy.		After onset of tetany.		Presence of sugar in urine unrelated to its administration.	Result.
	No. of observations.	Average tolerance in gm. per kilo.	No. of observations.	Average tolerance in gm. per kilo.		
A-167	4	8 to 9			On 11th day	Fatal.
A-183	4	9 to 10	8	2 to 3		Not fatal.
A-208	4	8	9	2 to 3	Negative	Fatal.
A-210	2	7 to 8			On 5th day	Fatal.
A-213	4	6 to 7	3	2 to 3	Negative	Fatal.
A-217	20	2 to 3	5	2 to 3	On 3d day	Not fatal.
A-212	5	6 to 7	1	4	Negative	Not fatal.
A-214	3	9	3	2	Negative	Not fatal.
A-226	13	5 to 6	6	4 to 5	Negative	Not fatal.
A-211	6	2 to 3	21	2 to 3	On 3d day	Not fatal.

It is seen from the above table that in adult bitches great differences (varying from 9–10 to 2–3 grams per kilo) occur in the natural tolerance from glucose. This must be determined separately, therefore, for each dog. In eight of the ten cases a considerable fall was noticed after parathyroidectomy, while in two with naturally low assimilation limits the tolerance remained unchanged after the removal of at least three parathyroids. The feature of most interest is that parathyroidectomy does not result in constant glycosuria. MacCallum and Voegtlin (27) reported constantly negative results. Such dogs on the average are capable of assimilating from two to three grams per kilo without its appearance in the urine, and more than this quantity is occasionally not tolerated by dogs with intact parathyroids. This suggests that the parathyroids are only a part of a system controlling sugar metabolism. The thyroids were in all these cases slightly goitrous and, for the most part, removed along with the parathyroids, but from data to be published later regarding thyroid and sugar tolerance we have concluded that the presence or the absence of the thyroid has little or nothing to do with this acute change in alimentary sugar tolerance. The administration of calcium salts does not seem to modify the altered sugar tolerance of parathyroidectomy.

CALCIUM SALTS IN TETANY.

Calcium salts are palliative and preventative, but in no sense curative. MacCallum and Voegtlin (27) have shown that in nearly all cases of parathyroid tetany calcium salts introduced by mouth or intravenously quickly but temporarily relieve the tetany. In this series there was one case where large quantities of calcium chloride by mouth failed to modify the symptoms, and later intravenous injection of considerable quantities likewise failed to modify the symptoms materially. Such cases must be exceedingly rare, however. After total parathyroidectomy calcium salts tend to, and in most cases do, prolong life. The mechanism of its action is unknown. There were several cases in the series that lived 8, 10, 15, and even 20 days with the aid of calcium salts, that as experience has shown usually die in a few hours or a few days. On the other hand our observations have shown that in cases where a remnant of active parathyroid tissue remains, calcium salts will permanently save such animals which otherwise would succumb to violent tetany. In our series of thirty-eight, four (A–121, A–148, A–183, and A–217) were surely saved by this means. Two others that died of fatal tetany (A–104 and A–115) could in all probability have been saved by the use of calcium salts for a few days as compressed but not necrotic parathyroids were found at the superior pole at autopsy. In tiding over otherwise fatal tetanies, therefore, calcium salts are of the greatest value. This fact is of clinical importance in operations on goitre in man. Total destruction of the parathyroids in the operation for human goitre should not occur except in the most extensive dissections for old complicated goitres and tumors, while partial destruction (the IVth on the given side) normally occurs when lobectomy is performed. The destruction of one or even two under normal conditions in man or dogs produces no untoward effects. When tetanies develop following operations calcium salts are of the greatest value in tiding over acute insufficiencies. The use of calcium is also of value in testing the completeness or incompleteness of the parathyroidectomy. If the operation is complete calcium will not permanently prolong life. As an example of the effect of calcium in prolonging life the following experiment is reported.

Dog A–121.—Middle-aged fox terrier; male. Apr. 20, 1908. Weight 7.3 kilos. Following the eleventh thyroid operation on Dec. 22, although 1 c.c. of saturated aqueous solution of calcium chloride was given just after the operation and another 1 c.c. dose on the following morning, he developed mild signs of tetany about noon and in the afternoon the dose was doubled. Dec. 24. Legs spastic, but the animal eats heartily and is able to move about. Weight 11 kilos. Dec. 27. Slight tetany. Dec. 29. Quite marked tetany; very ataxic. 3 c.c. saturated calcium chloride solution. Dec. 31. Slight twitching. Jan. 1, 1909. Well marked tetany; calcium chloride given. Jan. 2. Severe tetany; unable to stand; changed to lactate and given 10 c.c. of 5 per cent. solution daily. Slight signs of tetany each day occasionally reaching severe tetany until Jan. 8; then the dose was increased to 20 c.c. daily. Weight 10 kilos. Eats heartily. Exposure to cold appears to bring on tetany. Jan. 11. Slight tetany. Jan. 14. Marked tetany. Respiration 88. Pulse 180. Abdomen distended. Nose, ears, and feet hot. Jan. 15. A canine parathyroid was transplanted into the right rectus muscle. No calcium was given until Jan. 24, when slight signs of tetany appeared again. Calcium lactate was started again. Jan. 25. Slight tetany. Jan. 26. Violent tetany. Jan. 29.

Violent tetany. Feb. 1. Slight sign of tetany. Feb. 2. Tetany. 10 ox parathyroids given by mouth. Feb. 3. 30 parathyroids given by mouth; definite twitching. Feb. 4. 100 parathyroids given by mouth; twitchings; and in the afternoon tetany became severe and calcium chloride was given. Weight 10.4 kilos. Feb. 6. Slight twitchings relieved by calcium chloride. Feb. 8. Tetany. 50 c.c. of 5 per cent. solution of calcium lactate given. Feb. 9. Under ether one and one half sterile ox parathyroids were inserted into the right rectus muscle, 25 c.c. of calcium lactate being given at the end of the operation. Feb. 10, 11, and 12. Free from tetany. Feb. 13. Tetany. Evidence of gastric irritation, vomits frequently, considerable amounts of mucus. Given 50 c.c. of 0.5 per cent. solution of calcium chloride subcutaneously. Feb. 15. Tetany. Respiration 180. Pulse 210. Apparently suffering pain. Calcium lactate given in milk. Feb. 16. Mild tetany. It appears evident now that calcium salts are not well borne when administered by mouth. Feb. 18. Free from tetany. Calcium lactate given in milk. Feb. 19. The fourteenth operation for thyroid removal; much scar tissue about the remaining stump. The animal rallied quickly, ate heartily, and was given 50 c.c. of 5 per cent. solution of calcium lactate in milk about 6 P. M. Feb. 20, 8 A. M. Dead from hemorrhage.

Autopsy.—The hemorrhage is seen to be from the superior thyroid artery which had been cut almost flush with the carotid trunk, and the stump was too short to hold the ligature. Viscera are blanched. Two accessory thyroids, the size of small cherries, were found imbedded in the thymus. Chronic catarrhal gastritis, probably from calcium salts. The other tissues appeared normal. At the time of operation the dog seemed to be in perfect health, and was fat and sleek.

As regards the administration of calcium, the stomach route is preferable to all others and is equally efficient, since the few minutes' quicker action when given intravenously is offset by the greater dangers. Subcutaneous injection is also not to be recommended on account of the irritant action, discomfort, and danger of necrosis. In all our dogs gastric irritation was present. This could have been much lessened by giving the lactate of calcium in milk instead of the highly irritant calcium chloride which is more soluble and acts more quickly. Whether the daily use of calcium as bone would save such dogs is not known. Our few experiences with the temporary use of bone indicate that it also aids.

PARATHYROID OPOTHERAPY.

Unlike thyroid feeding in myxedema, the feeding of parathyroid glands by mouth has no influence over the course of tetany. MacCallum and Voegtlin (27) reported negative results from their experiments, and we have given as high as 100 fresh ox parathyroids daily to dogs with complete tetany without any amelioration of symptoms or prolongation of life. In another case (dog A–121) of incomplete but permanent tetany, ten ox parathyroids were given on one day, thirty on the following day, and 100 on the third day, also with negative results. In the same dog one canine parathyroid taken aseptically and inserted into the right rectus muscle maintained the dog free from tetany for eight days, and at the end of this period histological examination of the scar showed no evidence of the parathyroid. A large ox parathyroid was then inserted and this likewise relieved the tetany for five days. MacCallum (27) refers to an observation of Halsted's where feeding ox parathyroids by mouth seemed of value in a case of human tetany, although Shepard (28) reports negative results from a similar experience. MacCallum (29) and others have shown the rapid relief of symptoms by the intravenous injection of fresh parathyroid emulsions, and Beebe (30) has further shown that the parathyroid nucleoproteids also relieve tetany when introduced intravenously.

Transplantation is a difficult procedure and although there are many reports of successes the data of permanency are often incomplete. Halsted (31) points out the necessity of first creating a physiological insufficiency, but even then most of the attempts are failures. Our three attempts to transplant them into the rectus muscle were failures, although the dogs were temporarily relieved of tetany from five to eight days. Bone marrow, spleen, and thyroid are said to be more favorable sites for transplantation.

SUMMARY.

Accessory parathyroid tissue unassociated with the thyroid lobes is present in 5 to 6 per cent. of dogs. For the determination of the presence of accessory parathyroid tissue there are two tests: (1) the anatomical, often entailing serial sections of the neck and upper thoracic structures, and (2) the biological, consisting of the daily use of some calcium salt for two to three weeks. The latter is more easily carried out and more accurate. In the absence of all parathyroid tissue calcium salts will not save the animal's life, while in the presence of active parathyroid tissue calcium will save it. Many factors other than the amount of parathyroid tissue removed influence the onset of tetany, among which are age, pregnancy, lactation, rachitis, the administration of sulphur, and diet.

Pregnancy and lactation tetany in dogs resembles in all essentials parathyroid tetany. Our observations are in harmony with those who hold that the thyroid and parathyroid are independent structures as regards their anatomy, physiology, and pathology. The removal of the parathyroids immediately lowers alimentary sugar tolerance, but rarely to the degree of constant glycosuria.

In sharp contrast with thyroid substance in myxedema, the feeding of parathyroid substance fresh or dried by mouth is of no value in the parathyroid tetanies of dogs.

Calcium salts have a striking palliative effect on parathyroid tetany and preventative action in tiding over otherwise fatal cases, but are in no sense curative. The mode of action is unknown. There is some evidence that calcium salts directly influence the parathyroid gland.

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FURTHER OBSERVATIONS AND EXPERIMENTS ON GOITRE (SO CALLED THYROID CARCINOMA) IN BROOK TROUT (SALVELINUS FONTINALIS).

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FURTHER OBSERVATIONS AND EXPERIMENTS ON GOITRE (SO CALLED THYROID CARCINOMA) IN BROOK TROUT (SALVELINUS FONTINALIS).

III. ITS PREVENTION AND CURE.*

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PLATES 13 TO 17.

Investigations (1) made at the trout hatchery of the Blooming Grove Hunting and Fishing Club during 1909 and 1910 showed that all the fish were then goitrous. It was found that the thyroid hyperplasia began in the fry as soon as feeding was instituted, and advanced overgrowth was present at the fourth month of extra-oval life; that the overgrowth progressively increased to the stage of clinical detectability, as ascertained by the reddening of the pharyngeal floor over the thyroid area, about the tenth month in this hatchery; that visible goitres usually manifested themselves about the beginning of the second year, though they may be present as early as the sixth month, depending on the favorableness of conditions for overgrowth, and progressively increased during the second and third years; that older fish were more resistant and tended toward spontaneous recovery; that the water in which these fish lived was not naturally goitre-producing, since fish living wild in the stream and raceways did not develop thyroid overgrowth.

It was further shown that overcrowding and overfeeding with the highly abnormal and incomplete diet of hog's liver and heart were the major gross etiological factors, and of these the food was the more important factor in bringing about a fault of nutrition which stimulated the thyroid to compensatory overgrowth. No evidence was obtained that the disease was either infectious or contagious, or that a direct *contagium vivum* could account for the phenomenon.

The above summary of the work of 1909 and 1910 will serve as an introduction to the observations included in this report, which were made during August, 1913, and deal with the effect of changing the food from liver to fresh sea fish.

Comparison of the General Conditions Prevailing in 1909, 1910, and 1913.—The water supply has remained unchanged as regards source and volume (text-figure 1). The Club is holding more trout in each pond than in 1909 and 1910, hence the untoward factor of

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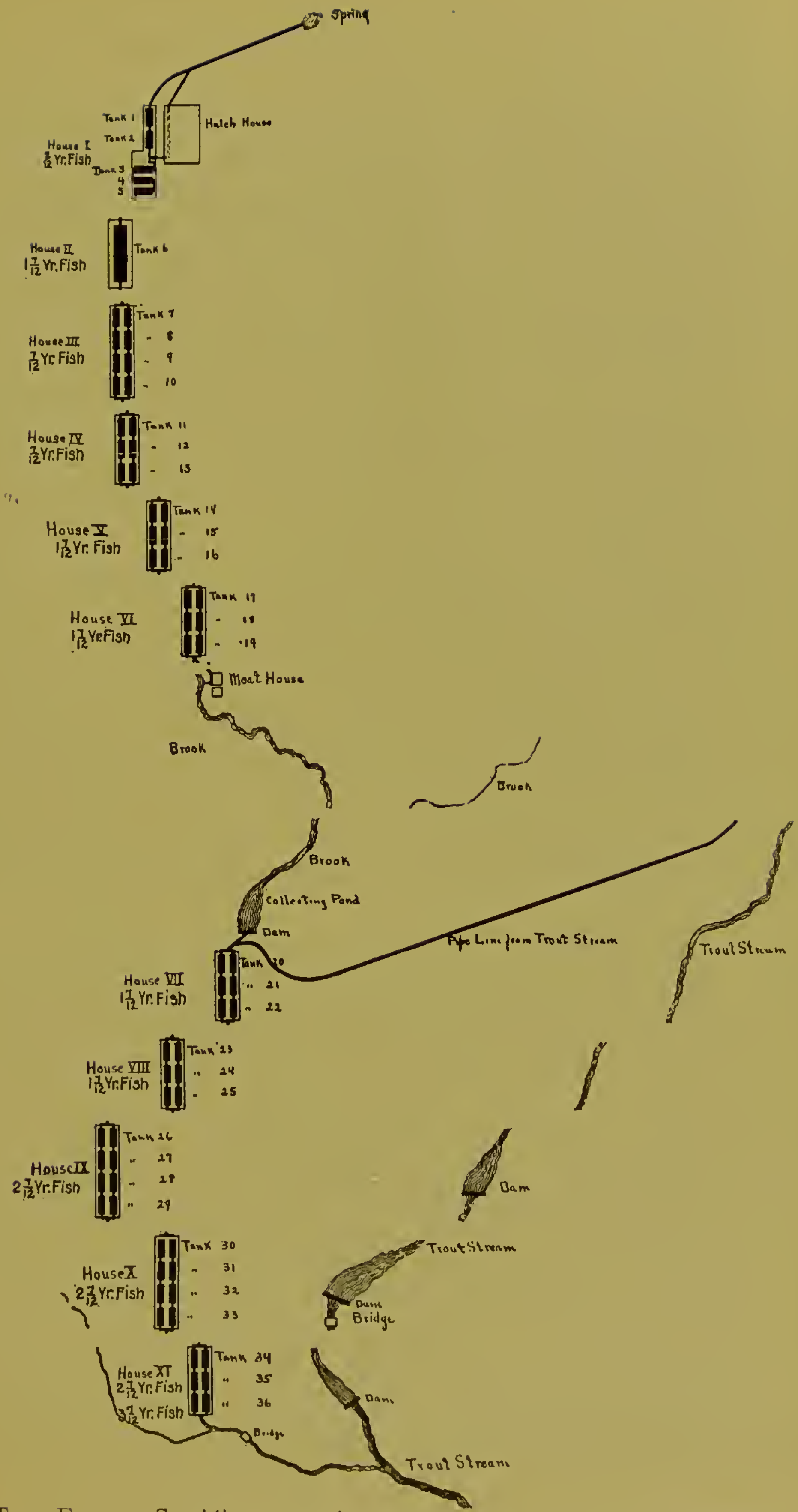

TEXT-FIG. 1. Semidiagrammatic drawing of the plan, arrangements, and location of the hatchery, water supplies, houses, and retaining tanks.

overcrowding is increased. The distribution of the fish is in general the same (text-figure 1),—the fry (hatch of 1913) in the upper, the nineteen months old trout in the middle, and the thirty-one months old trout in the lower ponds. The fry have always been scrupulously cared for by daily cleaning and sweeping the troughs and ponds. With the older fish (nineteen and thirty-one months) there is clearly less detritus in the ponds than in 1909 and 1910, although little additional attention has been paid to these ponds, the difference being due mainly to the change of food. Therefore, apart from the increased number of fish being held in the same pond space and the water supply, the only important change has been in the food.

The Food.—Beginning with October, 1911, fresh sea fish (butter fish (*Stromateus triacanthus*) and occasionally weak fish (*Cynoscion regalis*)) have been fed six times weekly to the older fish to the exclusion of all other foods. The fry are fed two to three times daily as in previous years, with finely divided hog's liver for the first four to five months of life, then heart muscle (hog) is added to this diet. This is continued until October (*i. e.,* nine months), when all the fry are removed to the ponds. At this time the change to fish diet is also made and maintained during the remainder of their stay in captivity.[1]

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[1] It is as yet impossible to change to the fish diet earlier than the ninth month on account of the inability to hash the fish finely enough with the present machinery. This will soon be remedied, however, and then much of the thyroid overgrowth that now occurs during the period of liver feeding will be prevented. Several kinds of fish have been tried as food, among which are sea bass (*Centropristes striatus*), herring (*Clupea harengus*), weak fish (*Cynoscion regalis*), and whiting (*Merlangus americanus*). All have been found unsuitable either on account of bones or scales and have been abandoned. The fish scales being unaffected by digestion form rouleaux in the gut and produce intestinal obstruction followed by the usual sequelæ of enteritis, distention peritonitis, and death. I had the opportunity of examining two mild cases of partial intestinal obstruction, although for the past year only an occasional large scaled fish has been included in the food. In the two fish examined the obstruction was intermittent, as the scales were small (from weak fish) and could only obstruct when arranged transversely in the gut. There was well developed enteritis of the straight gut with extension through to the mesentery. Bones, if fine and rigid as in herring, are not broken up by the hasher and often perforate the stomach wall before the gastric acid can decalcify them. Fish with cartilagenous endoskeletons, such as skates, rays, sharks, etc., have not been tried owing to the difficulty as yet in

Comparison of the Gross Appearance of the Fish of 1913 with Those of 1909 and 1910.—Very striking differences are apparent. The nineteen months and the thirty-one months old fish are active and alert, while those of corresponding ages in 1909 and 1910 were sluggish and lumbersome. In handling large numbers of them in each of these three years, the 1913 fish are clearly stronger, show more fight, fatigue less easily, and do not die so quickly when removed from the water.

The fish are now more trout-shaped, that is, they have lost the pot-bellied appearance of 1909–1910. The skin pigments are brighter and better differentiated. It will be recalled from the descriptions of 1909–1910 that in all the fish the black pigment was excessively developed. The greenish grey marbling of the back was absent and the orange and pink color spots of the sides were wholly invisible. So also the orange and yellow colors of the fins and ventral surface were nearly absent. The silvery sheen of the sides was masked by the black pigment. In the fish of 1913 the colors approach closely those of the normal trout. The greenish marbling of the dorsum is detectable. The lateral color spots are well differentiated and the yellow and orange pigment of the ventral surface and fins are developed. The silvery sheen of the sides is perhaps better developed than in the average wild trout.[2]

As regards weight I have no exact data, although the impression is distinct that they are a trifle smaller on the average than in 1909 and 1910. The fry of 1913 are to all appearances the same as on previous examinations.

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obtaining them in the markets. There seems no objection to their use since they would obviate the two great objections, scales and sharp perforating bones, and in addition might be less expensive than the usual market fish. Butter fish (*Stromateus triacanthus*) have been found least objectionable of the obtainable fish and are now used almost exclusively. They are received frozen and therefore in better condition than usually obtains with liver.

[2] These colors being readily adaptable to environment are modified by the color of the water, hence native trout from the brook are slightly darker than trout living in the spring water of the hatchery. It may also be recalled that in the experiments of 1910 the excessive black pigment diminished rapidly upon changing the food and removal of the fish from the ponds to troughs or to the trout stream. It would therefore appear that the food was a factor in the excess of the black pigment developed.

Of other diseases independent of goitre, as the myxosporidian infection (Taumelkrankheit, cramps), fungus, and enlarged gills (so called sore gills), there is a definite decrease.

Comparison of the Gross Thyroid Condition of 1909 and 1910 with That Obtaining in 1913.—These data are obtained from the clinical examination of the thyroid areas of a series of fish from the ponds for the presence of (*a*) reddening of the pharyngeal mucosa between the first and third gill segments as the first clinical evidence of thyroid overgrowth, and for (*b*) visible goitres projecting either dorsally in the floor of the mouth or in the gills, or ventrally in the angle of the attachment of the operculum as a late sign. The fry were not thus examined.

TABLE I.

	October 12, 1909.				June 27, 1910.				August 10, 1913.			
Pond No.	Age in yrs.	No. of fish examined.	Reddening of pharyngeal mucosa.	No. with goitre.	Age in yrs.	No. of fish examined.	Reddening of pharyngeal mucosa.	No. with goitre.	Age in yrs.	No. of fish examined.	Yellowish discoloration of pharynx.	No. with goitre.
6					1.5	41	10	0	1.7	25	1? trace	0
14					1.5	51	45	1	1.7	32	2? trace	0
19	1.8	210	197	7	1.5	60	51	2	1.7	22	2 trace	0
20	1.8	210	175	3	1.5	54	40	0	1.7	30	0	0
21									1.7	25	0	0
25	1.8	67	61	2	1.5	48	41	1	1.7	24	1 trace	0
26									2.7	22	3 trace	0
32	2.8	60	58	2	2.5	50	38	1	2.7	29	3 trace	0
35					2.5	40	28	2	2.7	32	4 trace	0
36	1.8	210	183	4					3.7	16	3	0
Totals		757	89%	0.23%		344	74%	0.17%		257	0.07%	0.0%

From the above tabulation it is seen that in 1909 89 per cent. of the fish had distinct reddening of the pharyngeal floor, and 0.23 per cent. had visible goitres. In 1910 a similar examination of fish from the same ponds and of nearly the same ages showed distinct reddening of the pharyngeal floor in 74 per cent. and visible goitres in 0.17 per cent. In 1913 a third examination of the fish from the same ponds and of approximately the same ages as those of 1909 and 1910 showed only a slight yellowish discoloration of the pharyngeal floor[3] in 0.07 per cent., and visible goitres in none.

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[3] The reddening of the pharyngeal floor is due to the vascular thyroid tissue growing up to the pharyngeal mucosa. The yellow discoloration of the same region is due to the thyroid follicles rich in colloid and decreased vascularity, *i. e.*, recovery or colloid stage of a preceding hyperplasia.

These percentages illustrate the average condition of all the fish at the time of the examinations and are controlled by the histological examination of specimens removed at the same time from all the ponds during each of these years. The differences in the gross condition of the thyroids for the years 1909 and 1910 are unimportant but illustrate the severity and extent of the disease. The differences in the thyroid conditions of 1909–1910 and of 1913 were beyond what I had expected and demonstrate clearly that the disease in the 1913 fish had been completely arrested. There were none with reddening of the floor of the pharynx nor with goitre, hence none with any active overgrowth of the thyroid. The few instances where slight yellowish discoloration was present is indicative of colloid-filled follicles beneath the mucosa. How can this most striking difference in the thyroid condition be accounted for? The only noteworthy determinable factor of difference between the conditions prevailing in 1909 and 1910 and those of 1913 is the food,—sea fish in 1913 and liver in 1909 and 1910. That the change of food accounts for the differences in the thyroid condition will become more apparent from the following observations and comparisons of the histological conditions of the thyroids of the entire pond series for the three years.

Observations on the Histological Condition of the Thyroids from Specimens from All Ponds.—(Figures 1, 2, and 3, and table II.) For comparison I have tabulated the anatomical state of the thyroids in 1909 and 1910 with that of 1913. In this table all the fish are included: (1) the fry, (2) the one to two years old, and (3) the two to three years old fish.

In the case of the fry for 1909–1913, all conditions, including food, water, crowding, cleaning, and general hygienic conditions are as nearly identical as it is possible to keep them. This is most fortunate in that it makes comparisons of the thyroid conditions for each year possible under constant conditions. It also gives a broad foundation for estimating the average thyroid hyperplasia present in the fry and is therefore valuable for checking any changes found in the older fish. With the one to two years old trout and the two to three years old trout of 1913 all conditions except the food are similar to those of 1909 and 1910. The one to two years old trout of 1913 have been fed sea fish for the past ten months. The two to three years old trout have been fed sea fish for twenty-two months, while the one to two years and two to three years old trout of 1909 and 1910 had been fed with liver only.

All the fry of 1909, 1910, and 1913 exhibited the same general thyroid condition of active hyperplasia (figures 4, 5, and 6). The thyroid area is completely filled with thyroid tissue and extension to the adjacent bone and muscle is present in all. The differences in the different years are only of slight degree and are probably dependent on the slight age differences at the time of examination: 1909, 8 to 9 months old; 1910, 6 months old; 1913, 7 months old. The individual variations within a given year are also slight and in general the same for all years. The examinations in each year comprised two specimens taken without choice from the twenty-one troughs in the hatch house and thirteen pairs of ponds of the pond series for the fry and also two specimens for each pond of the remaining twenty-three pairs for the older fish. From the examination of the fry in 1910, which, in addition to the above, included a series taken at weekly intervals from the time of hatching (January 15) to October, it was shown that the thyroid overgrowth began as soon as the fish began feeding and was easily detectable at the fourth month of extra-oval life, whence it progressively increased through the following months of the first and second years, rarely becoming clinically detectable before the tenth month at this hatchery. In some hatcheries the overgrowth has been clinically detectable at the sixth to the seventh month, depending on more favorable conditions for thyroid overgrowth. The fry of 1911 and 1912 were not examined, but these same fish were included in the 1913 examination as thirty-one months and nineteen months old fish, respectively, and from this examination there is complete evidence that their thyroids had undergone changes identical with those in the years 1909, 1910, and 1913. Passing now to the nineteen months old fish, one finds a most striking change also noted in the gross examination of the thyroid area. All the follicles are in the colloid state, although their distribution extends into the bone and muscle and often up to the pharyngeal mucosa. The fish from the same ponds and of approximately the same age in 1909 and 1910 all had well marked active hyperplasia (figures 7 and 8) greater in amount and more widely distributed in muscle, bone, gills, and pharyngeal mucosa than those of 1913.The growth in nineteen months old fish of 1913 (compare figures 9 and 10 with figures 11 and 12) was found to be completely arrested, and the hyperplasia had completely involuted, while in the fish of 1909 and 1910 of the same age the growth was extending rapidly. As the arrest of the growth corresponds in time with the change in food, and as no other factor of difference is present, one is forced to the conclusion that the food is the major cause of the change. While the fish have grown rapidly during the ten months since the feeding of fish began, their thyroid tissue is no greater in amount nor more extensive in distribution than that reached during the first ten months of life. So also with the thirty-one months old fish which have been fed fish for twenty-two months the thyroids are completely involuted to the colloid state and the amount and distribution of the follicles are the same as those of the nineteen months old fish, and hence no greater than that attained during the first ten months of life, although the fish have made their normal annual growth. One sees, therefore, fish nineteen months and thirty-one months old with thyroids identical in all particulars and no greater in amount nor more extensive in distribution than those of liver-fed fry of ten months in this hatchery. That the growth was arrested and involution started at the time of the change from liver to sea fish cannot be doubted, although for the sake of completeness it will be necessary to make a series of weekly examinations beginning before and continuing for some months after the change of food to fresh sea fish. This is now being done. Additional proof that change

TABLE II.

Pond or trough No.	Age of fish in months.	1909.		Age of fish in months.	1910.		Age of fish in months.	1913.	
		Condition of thyroid.			Condition of thyroid.			Condition of thyroid.	
		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification.
Trough 1	8	All subpharyngeal structures,—bone and muscle	Marked hyperplasia	6	Entire aortic area; no invasion of bone or muscle	Moderate hyperplasia	7	Entire aortic area; invasion of bone and muscle	Marked hyperplasia.
Trough 5	8	All subpharyngeal structures,—bone and muscle	Marked hyperplasia	6	Entire aortic area: no invasion of bone or muscle	Moderate hyperplasia	7	All subpharyngeal structures in bone and muscle	Marked hyperplasia.
Trough 10	8	Entire aortic area including bone and muscle	Marked hyperplasia	6	Entire aortic area; invasion of bone and muscle	Marked hyperplasia	7	All subpharyngeal structures in bone and muscle	Marked hyperplasia.
Trough 15	8	Entire aortic area including bone and muscle	Marked hyperplasia	6	Entire aortic area; invasion of bone and muscle	Marked hyperplasia	7	Entire aortic area	Moderate hyperplasia.
Trough 20	8	Entire aortic area including bone and muscle	Marked hyperplasia	6	Entire aortic area; invasion of bone and muscle	Marked hyperplasia	7	Entire aortic area	Marked hyperplasia.
Normal above all ponds	20	Scattered follicles about aorta, filled with colloid	Normal	18	Scattered large follicles in aortic area, filled with colloid	Normal	19	Scattered large follicles in aortic area filled with colloid	Normal.
Pond 1	8	Entire thyroid area packed with follicles, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled; invasion of bone and muscle	Marked hyperplasia	7	Entire aortic area filled; invasion of bone	Moderate hyperplasia.
Pond 2	8	Entire thyroid area packed with follicles, in bone and muscle	Marked hyperplasia	6	Thyroid area filled	Moderate hyperplasia	7	Entire aortic area filled; invasion of bone	Moderate hyperplasia.
Pond 3	8	Entire thyroid area filled	Moderate hyperplasia	6	Thyroid area filled; invasion of bone	Moderate hyperplasia	7	Entire aortic area filled; invasion of bone	Marked hyperplasia.
Pond 4	8	Entire thyroid area filled	Moderate hyperplasia	6	Thyroid area filled; invasion of bone	Moderate hyperplasia	7	Entire aortic area filled; invasion of bone	Moderate hyperplasia.
Pond 5a	8	Entire thyroid area filled	Moderate hyperplasia	6	Thyroid area filled; invasion of bone	Moderate hyperplasia	7	Entire aortic area filled; invasion of bone	Moderate hyperplasia.

TABLE II.—*Continued.*

Pond or trough No.	Age of fish in months.	*1909.*		Age of fish in months.	*1910.*		Age of fish in months.	*1913.*	
		Condition of thyroid.			Condition of thyroid.			Condition of thyroid.	
		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification.
Pond 5b	8	Entire thyroid area filled	Moderate hyperplasia	6	Thyroid area filled; invasion of bone	Moderate hyperplasia	7	Entire aortic area filled; invasion of bone	Moderate hyperplasia.
Pond 6	8	Entire thyroid area filled	Moderate hyperplasia	18	Entire thyroid area filled, in bone and muscle; infoldings; no colloid	Marked hyperplasia	19	Numerous small and large colloid-filled follicles in entire thyroid area	Colloid goitre.
Pond 7	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire thyroid area filled, in bone	Moderate hyperplasia	7	Aortic area filled; extension to bone	Moderate hyperplasia.
Pond 8	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 9	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 10	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 11	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 12	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 13	8	Entire thyroid area filled, in bone and muscle	Marked hyperplasia	6	Entire aortic area filled, in bone and muscle	Marked hyperplasia	7	Aortic area filled; extension to submucosa	Marked hyperplasia.
Pond 14	20	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	18	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	19	Numerous colloid-filled follicles in entire aortic area	Colloid goitre.
Pond 19	20	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	18	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	19	Numerous colloid-filled follicles in entire aortic area	Colloid goitre.

Pond or trough No.	Age of fish in months.	1909.		Age of fish in months.	1910.		Age of fish in months.	1913.	
		Condition of thyroid.			Condition of thyroid.			Condition of thyroid.	
		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification.		Extent of overgrowth.	Classification
Pond 20	20	Entire subpharyngeal space filled, in bone and muscle	Colloid, moderate hyperplasia (hyperplasia involuting)	18	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	19	Numerous colloid-filled follicles in entire aortic area	Colloid goitre.
Pond 21	20	Entire subpharyngeal space filled, in bone and muscle	Colloid, moderate hyperplasia (hyperplasia involuting)	18	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	19	Numerous colloid-filled follicles in entire aortic area	Colloid goitre.
Pond 25	20	Entire subpharyngeal space filled, in bone and muscle	Colloid, moderate hyperplasia (hyperplasia involuting)	18	Entire subpharyngeal space filled, in bone and muscle; visible goitre	Marked hyperplasia	19	Numerous colloid-filled follicles in entire aortic area	Colloid goitre.
Pond 26	32	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia, small visible goitre	30	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	31	Numerous colloid-filled follicles in entire aortic area; number of follicles same as in 19 mos. old fish	Colloid goitre.
Pond 32	32	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	30	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	31	Numerous colloid-filled follicles in entire aortic area; number of follicles same as in 19 mos. old fish	Colloid goitre.
Pond 35	32	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia, slight general fibrosis	30	Entire subpharyngeal space filled, in bone and muscle; visible goitre	Marked hyperplasia	31	Numerous colloid-filled follicles in entire aortic area; number of follicles same as in 19 mos. old fish	Colloid goitre.
Pond 36	20	Entire subpharyngeal space filled, in bone and muscle	Marked hyperplasia	30	Entire thyroid area filled, extension to skin, bone and muscle	Marked hyperplasia	43	Entire subpharyngeal area filled with colloid follicles, in bone and muscle; number of follicles much greater than in the 19 or 31 mos. old fish	Colloid goitre.

of food is the cause of the arrest of thyroid growth is the preservation of 250 forty-three months old fish which had been fed liver for the first twenty-one months of life and sea fish for the last twenty-two months. In these I found three out of the sixteen examined having distinct yellowish discoloration of the pharyngeal floor, and in the two specimens examined histologically the thyroid was completely involuted to the colloid state; but the amount and distribution were far more extensive than in the thirty-one and nineteen months old fish, showing that the thyroid overgrowth had progressed much farther before the involution began, and corresponds to the extra year of liver as food.

It is well known that foods influence the mammalian thyroid to a marked degree. Baumann (2) noticed that flesh diets stimulate the thyroid in dogs to active hyperplasia. I have repeatedly made such observations, liver being the most important food in this regard. Reid Hunt (3) in his acetonitrile experiments noted that liver stimulates the thyroid of white mice. Watson (4) has described the effect of different diets on rat thyroids and also noted that meats produce hyperplasia, while mixed diets do not. I have made similar observations. Dogs spontaneously recover from goitre on a mixed diet, while meats, especially liver, maintain hyperplasias. In zoölogical gardens where carnivores are held and bred in captivity and the diet is for the most part beef, goitre, rickets, and osteomalacic states are quite common. Foods modify the thyroid slowly, involution extending over months, while iodin involutes hyperplasias much more rapidly. Iodin administered to dogs, sheep, pigs, and human beings often induces involution in a month, and in Lake Erie pike the involution of mild degrees of hyperplasia takes place in twenty-six days (5). In brook trout with extensive thyroid overgrowth and visible goitres involution occurs in forty days.

To summarize, it is seen that the ages of the fish held at the hatchery in August, 1913, are seven months, nineteen months, thirty-one months, and forty-three months. The seven months old fry all have active hyperplasia not different in degree or extent from the fry of 1909 and 1910. The nineteen, thirty-one, and forty-three months old fish all have completely involuted or colloid thyroids, and the amount and distribution of the thyroid tissue in the nineteen and thirty-one months old fish are the same and represent the degree of thyroid overgrowth reached during the first nine months of life when liver and heart only are fed. The forty-three months old fish had been fed with liver and heart for the first twenty-one months of life, and the thyroids both on gross and microscopical examinations were much larger and more widely distributed than in the nineteen and twenty-one months old fish.

DISCUSSION.

These data afford supplementary proof for several of the conclusions deduced from the earlier work, and in addition establish another simple and certain means for the cure and prevention of goitre in fish.

The view previously held by some observers that this disease was closely related to true carcinoma is now only of theoretical interest, since, in addition to the facts already reported, it establishes the fact that the feeding of fresh sea fish also readily arrests the disease. No tissue overgrowth that presents the biological phenomena described for this disease, which are also identical with those of mammalian goitre, can be considered malignant. It was urged by some observers that the reaction with iodin could not be utilized as proof that the disease was not cancer since arsenic, mercuric chloride, and colloidal copper were reported to have the same thyroid effects (6). I have not been able to affect these changes with arsenic in canine goitre. I (7) have also failed to modify the growth of the mammalian thyroid carcinoma by the use of iodin, and from an extensive experience with human thyroid adenomata the conclusion was reached that they also are rarely affected by iodin (8). On the other hand, simple physiological hyperplasias of all animals are readily and invariably modified by iodin.

This disease should be classified as endemic goitre or endemic thyroid hyperplasia. One must recognize all degrees of the overgrowth in fish, just as in mammals, from the slightest departure from normal, detectable only microscopically, to the most extensive infiltration of the thyroid region and the formation of external goitres. Whether this form of goitre is similar to ordinary goitre in birds and mammals is not known. As mentioned above, they are identical anatomically, physiologically, and pathologically in all their known reactions, but inasmuch as goitre is only the symptomatic manifestation of a nutritional disturbance it is possible that many agents are capable of exciting the thyroid to this single and only known anatomical manifestation of increased activity, compensatory hypertrophy and hyperplasia.

From our knowledge of mammalian goitre it would seem probable that the thyroid reaction in infectious diseases, puberty, pregnancy, cretinism, Basedow's syndrome, etc., are not due to the same exciting cause. The fundamental fault in nutrition is probably the same in all, but the immediate exciting agent is probably different. In mammalian goitre the localization in certain districts is most obvious, while in fish and in birds this is not so apparent although it is present. Goitre, however, occurs wherever favorable conditions are created whether in mammals or in the lower animals. It is therefore the increased susceptibility of mammals to goitre that brings out the localization of endemicity. Fish are very resistant to goitre and only acquire the disease when subjected to conditions incompatible with prolonged life in mammals.

The nearest approach to the etiology of goitre in fish was made when it was shown that food is the major etiological factor. Fish fed exclusively with liver always acquire thyroid hyperplasia, while fish of the same age, breed, and environment readily recover or escape goitre when fed with whole sea fish.

It is almost certainly a biochemical reaction, but whether it is due to the presence or absence of some substance normally needed by the organism is not known. A comparison of liver as a food with fish as a food seems to indicate that the liver lacked something normally needed by the developing fish which the diet of fish contained.

It is also probable that the liver contains some substances in excess, in attempting to utilize which, the animal exhausts other elements necessary for nutrition which are not present in the liver in sufficient amounts. As to the nature of this chemical fault one cannot reasonably speculate. From time to time most of the inorganic and many of the organic substances have been specified as etiological factors, but without foundation. Some observers have called it a toxin, but work based upon this hypothesis has added nothing to our knowledge of the etiology.

Iodin is certainly reduced in fish with thyroid hyperplasia, as in all other animals, and iodin certainly prevents and involutes hyperplasia, but the conclusion that goitre is due to a deficiency of iodin is not justified since there is considerable evidence to show that some other factor or factors are operating to divert or deplete an otherwise sufficient amount of iodin. On the other hand, the beneficial effects of feeding fish may be due to the iodothyreoglobulin that it contains, since only exceedingly small amounts are necessary, and the whole fish including the thyroid gland is used. Sea fish may also contain traces of iodin apart from the thyroid. Therefore much careful work must still be done to exclude iodin as the cause of the beneficial effects. I have made two iodin determinations on mixed specimens of whole butter fish, and two determinations on mixed specimens of fish from which the thyroid areas had been removed. The results are as follows: (1) whole fish, slightest trace; (2) exclusive of thyroid area, no trace of iodin.

The possibility of a *contagium vivum* in fish goitre can, it seems to me, be eliminated since there is not the slightest evidence that it is either contagious or infectious. It obeys none of the laws which we associate with true infectious processes. No evidence of natural or acquired immunity has been obtained, though different species of fish exhibit different degrees of resistance (carp, trout).

Gaylord (9) has reported the finding of evidences of immunity, but this evidence does not exclude the following important factors: (1) Age is an important factor in all animals; the young are more susceptible to goitre and the old tend toward spontaneous recovery. (2) When the active hyperplasia involutes to the colloid state it is more difficult to produce again active hyperplasia (*a*) because of the increased age of the animal, and (*b*) because of the increased factor of safety due to the increased number of thyroid follicles over what obtains normally. For example, if a dog has fifty grams of colloid thyroid it is more difficult, apart from any age factor, to induce active hyperplasia in it than if the dog has three grams of normal thyroid; but other things being constant, three grams of colloid will undergo hyperplasia as readily as three grams of normal thyroid. (3) The food is probably the most important factor in determining the onset or cessation, progression or regression of the hyperplasia. (4) Water supply has some influence on the resistance of fish to active hyperplasia, reduced and much used water favoring, and large amounts lessening it. (5) The different Salmonidæ vary greatly in their susceptibility. I have seen none that were not susceptible, but the brown trout and rainbow trout in my experience have been more resistant than the silver salmon or brook trout.

The water supplied to this hatchery has little if anything to do with the development of goitre, since the fish have never developed the disease unless the single factor of overfeeding with the highly abnormal diet of liver and heart is also operating. The following observations bearing on the relation of water to the etiology and spread of goitre may be mentioned: (1) Within the hatch house are twenty-one troughs,—twelve hatch troughs and nine nursing troughs. The twelve hatch troughs receive water directly from the spring, while the nine nursing troughs receive the water from the twelve hatch troughs. Every summer these troughs are used to hold extra fry. They are kept remarkably clean, yet all the fry have shown equally marked thyroid overgrowth in each of the years that they have been examined. Fish living outside the troughs and ponds (hence not directly fed with liver), whether above, below, or between the troughs and ponds, never develop active hyperplasia, although in most instances they have some degree of colloid goitre, showing that they had once been confined in the troughs or ponds and that, after escaping, the hyperplasia involutes. (2) The 1913 distribution of the fish made another observation possible. In house II (text-figure 1) there are 3,000 nineteen months old fish which have been fed with fish for the past ten months; all these fish have colloid glands. While above in house I and below in house III there are seven months old fry which have been fed only with liver and heart muscle and all have well marked active thyroid hyperplasia. There is also some evidence that liver when fed in excessive amounts is a more potent stimulus than when fed in small amounts, as the fish living in the runways between the houses also obtain small particles of liver which float through the screens but do not develop active hyperplasia. Plehn (9) has reported greater variations in the occurrence and distribution of the disease in a fish hatchery than they could account for purely on the basis of external changes. They suggest that these variations point to infection. I have also seen wide variations in its occurrence in different hatcheries and even in the same hatchery, but feel that all the variations could be accounted for on the basis of one or more of the following factors: (1) food, (2) water supply, (3) age, and (4) species of fish. Some observers have applied the term epidemic goitre to this form of goitre in fish. This is wrong. There is nothing acute or localized in its occurrence or distribution. It appears wherever fish are overfed with liver or other incomplete foods. It extends over the entire time of such feeding and all fish are affected.

Goitre has been present in this hatchery for the past twenty-five years and, in my opinion, it will remain as long as fish of any age are fed with liver.

Treatment and Prevention.—Trout living in their normal environment and partaking of their normal food do not develop goitre, hence in the treatment and prevention our efforts should be directed toward imitating natural conditions as far as possible. However, as with many other animals it has been found possible to alter these natural environmental conditions within extremely wide limits without seriously impairing their health. Goitre is one of the serious diseases that has developed in testing the range of adaptability. The infectious diseases of fish, as of mammals, are better known and methods for the cure and prevention have been studied longer. Goitre belongs to the group of diseases dependent upon nutritional disturbances, and our knowledge of the food requirements of animals generally and of fish in particular is as yet in its infancy.

It has been conclusively shown that the feeding of the highly artificial and incomplete diet of liver and heart muscle is the major factor in the causation of fish goitre, and the first essential in treatment is to provide some other food that meets the animal's requirements. A natural food of trout is fish and the experiments of the past two years show that when sea fish is fed to these trout existing goitre is cured and the development of goitre is wholly prevented.

The feeding of fish with hard fine bones or with large heavy scales is associated with risks mentioned above. The fish stomach is adapted for the ingestion of relatively large food boli, and food should be fed in as large masses as they will take since digestion is a continuous process in fish. This would probably solve the bone question and would tend to control overfeeding. Some sort of chopper should be devised instead of hashers, since hashers mince the food and allow of too rapid digestion and, therefore, too long intervals of stomach inactivity. Coarse fish, like sharks, rays, etc., might be utilized. Sea fish, therefore, makes a perfect food as far as the cure and prevention of goitre are concerned. Overfeeding must be guarded against. Definite amounts of food should be fed but once a day with a fast day each week comparable to the fast day maintained among the carnivores at Zoölogical Gardens. No observations have been made as to the minimum amounts of sea fish necessary to involute or prevent hyperplasia, but judging from the rapidity of the involution when the food is changed to fish only, it would appear that the daily feeding with fish was not necessary to cure or prevent the hyperplasia. It might be beneficial to alternate between fish and liver or between fish and other foods daily or weekly. Overcrowding is dependent on the water supply and the food. It is a highly important factor as regards the general health of the fish, the prevention of traumata and infectious diseases, the oxygen supply, etc., but is only a minor factor in the production of goitre.

Cleanliness likewise is a secondary factor in goitre, but is of great importance in the prevention of other diseases and as a general hygienic measure cannot be neglected. Modification of pond construction with this in view would greatly simplify the cleaning and sanitary problems. Iodin in minute traces has also been found to prevent and cure goitre. Indeed it is a specific therapy for goitre but does not relieve other untoward manifestations of an incomplete food. Gaylord (6) has reported that arsenic and mercuric chloride also effect similar changes in fish thyroid hyperplasia. Our observations with arsenic in canine goitre were negative and in any event the action of arsenic and mercuric chloride is not comparable to the action of iodin on the thyroid.

CONCLUSIONS.

1. Goitre in fish is a non-infectious, non-contagious, symptomatic manifestation of a fault of nutrition, the exact biochemical nature of which has not been determined.
2. Feeding the highly artificial and incomplete diet of liver is the major etiological factor in bringing about this fault of nutrition which is at once corrected by feeding whole sea fish.
3. Water plays no essential part in the etiology, transmission, or distribution of the disease in the fish of this hatchery.

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EXPLANATION OF PLATES.

PLATE 13.

FIG. 1. Rough projection sketch of a transverse section through the thyroid area of a brook trout with a normal thyroid.

FIG. 2. Rough projection sketch of a transverse section through the thyroid area of a brook trout with a mild degree of active hyperplasia.

FIG. 3. Rough projection sketch of a transverse section through the thyroid area of a brook trout with a mild degree of colloid (goitre) gland.

PLATE 14.

FIG. 4. Transverse section of the thyroid area of a five months old brook trout showing the extent of the thyroid overgrowth at this age in fry of the hatch of 1910.

FIG. 5. Higher magnification of figure 4, showing the filling up of the thyroid area, the extension to the cuticle, to the pharyngeal mucosa, and on the right the extension to the gill filaments. Note the relation of the follicles to the two terminal branches of the ventral aorta, the size of the follicles, the high columnar epithelium with infoldings and plications, and the absence of stainable colloid.

PLATE 15.

FIG. 6. Transverse section of the thyroid area of a seven months old brook trout of the hatch of 1913 showing the pharyngeal mucosa above and gill filaments laterally. Note the distribution of the hyperplastic follicles about the ventral aorta and their irregular distribution throughout the thyroid area.

FIG. 7. Transverse section of the thyroid area of a seventeen months old brook trout, showing the whole thyroid area uniformly filled with hyperplastic thyroid follicles.

PLATE 16.

FIG. 8. Higher magnification of an area from figure 7, showing the infoldings and plications, vascularity, high columnar epithelium, absence of stainable colloid, and the great distortions and variations in the size of rapidly growing thyroid follicles.

FIG. 9. Transverse section of the thyroid area of a nineteen months old brook trout which during the first nine months of life had active hyperplasia, and upon the introduction of fish as the food all the follicles involuted back to the colloid state. Note the distribution and numbers of follicles as those attained during the stage of active hyperplasia, while the individual follicles now resemble in all essentials normal follicles. Note also the extension into bone and muscle. This is the colloid, or resting, or cured stage of a mild degree of active hyperplasia.

PLATE 17.

FIG. 10. Higher magnification of a portion of figure 9, showing part of the ventral aorta and the large venous space to the left. Compare the numbers and distribution of the follicles, their colloid contents, and their epithelial investments with those of figure 12.

FIG. 11. Transverse section through the thyroid area of a nineteen months old brook trout, showing the pharyngeal mucosa above, gill filaments laterally, and scattered thyroid follicles of different sizes widely distributed about the ventral aorta. Normal thyroid.

FIG. 12. Higher magnification of an area from figure 11, showing the size and arrangements of the follicles together with the colloid contents and epithelial investments.

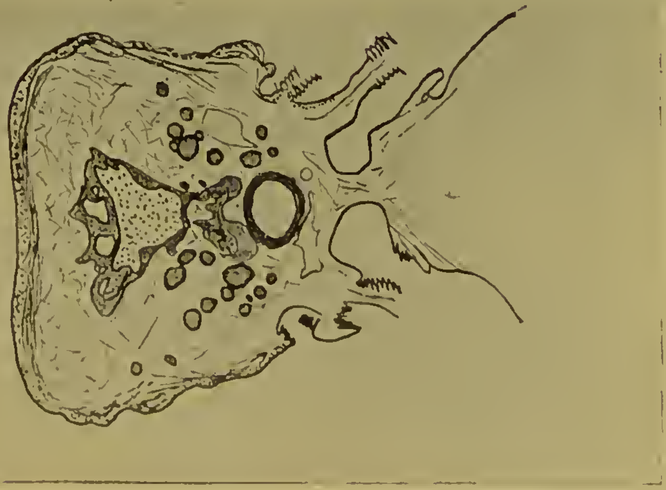

FIG. 1.

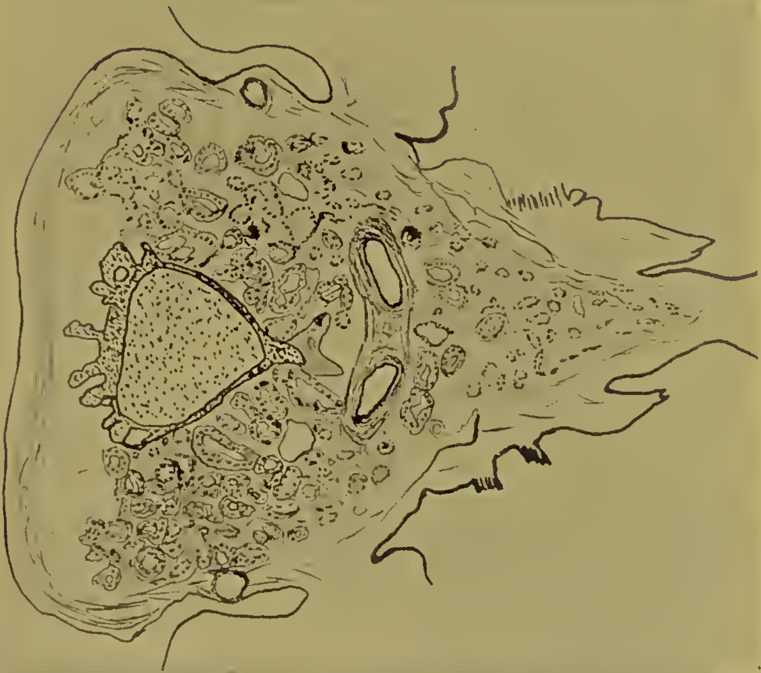

FIG. 2.

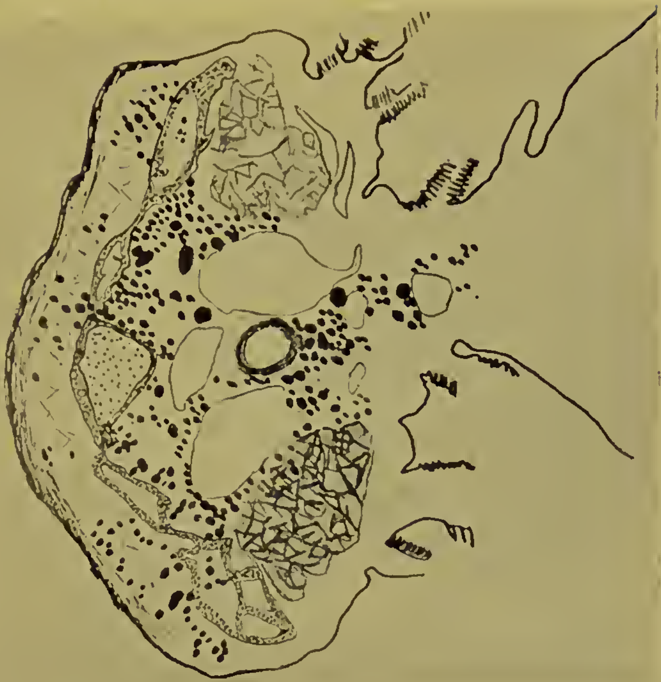

FIG. 3.

(Marine: Goitre in Brook Trout.)

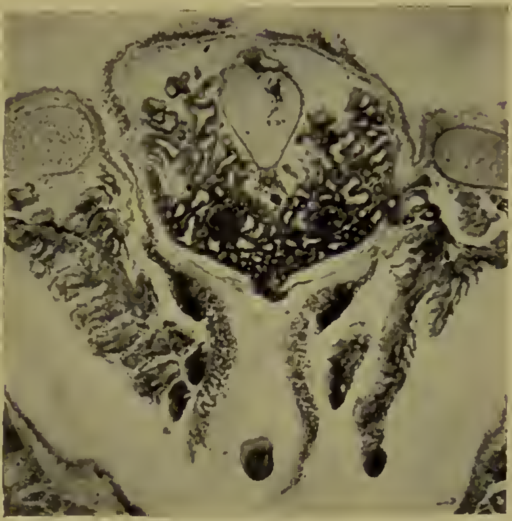

FIG. 4.

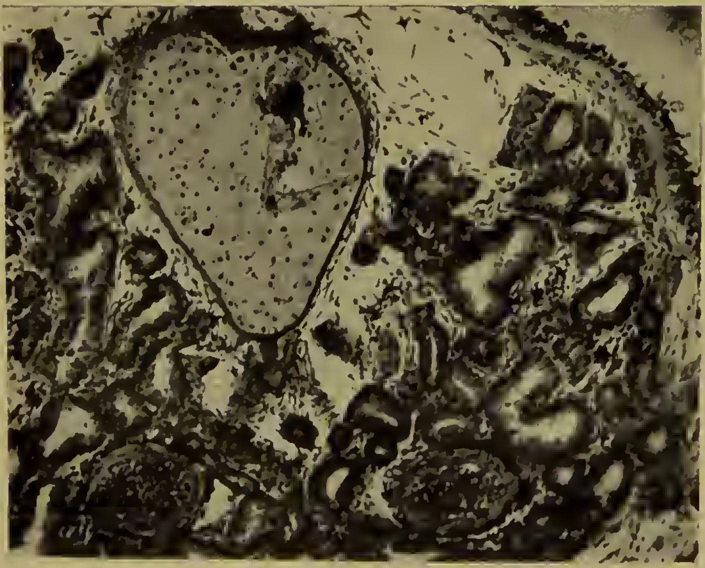

FIG. 5.

(Marine: Goitre in Brook Trout.)

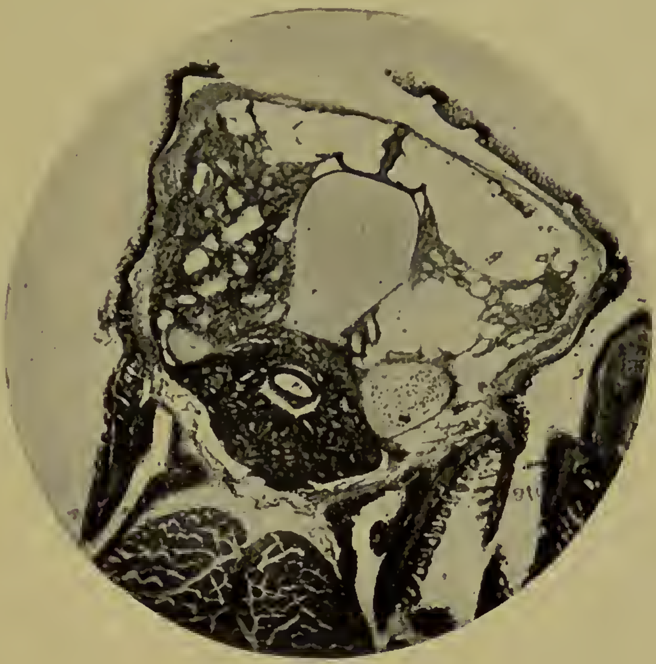

FIG. 6.

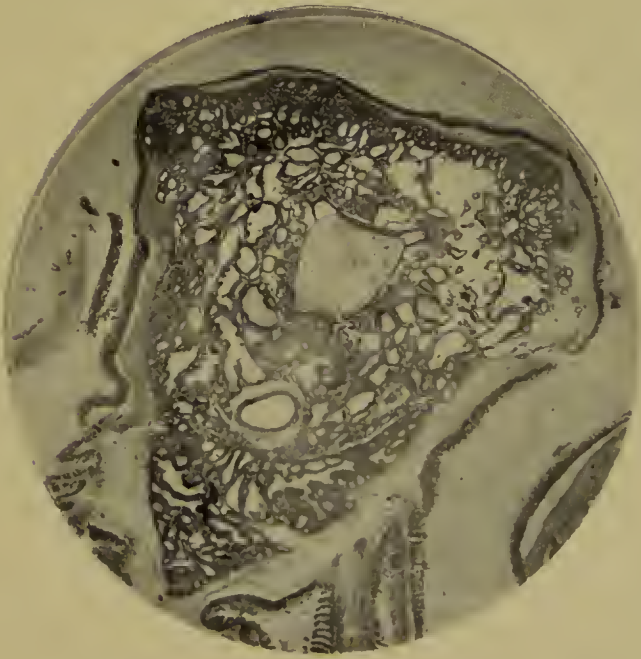

FIG. 7.

(Marine: Goitre in Brook Trout.)

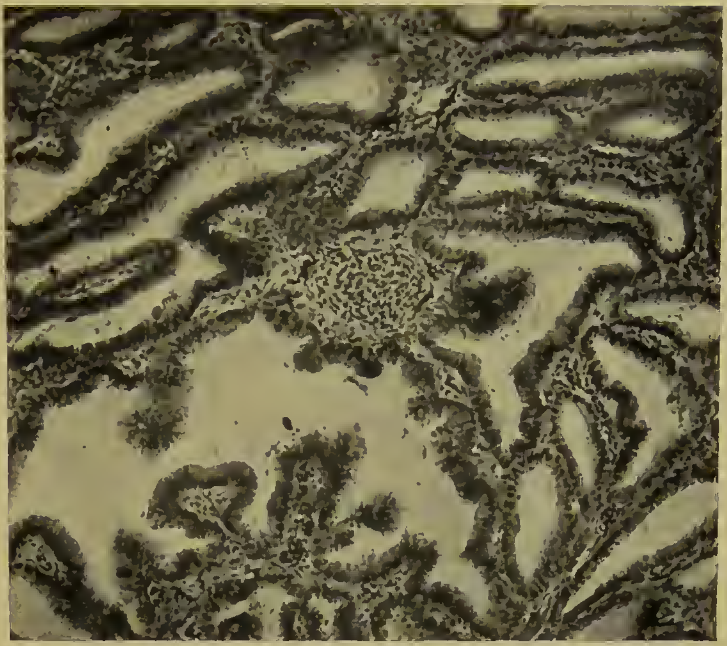

Fig. 8.

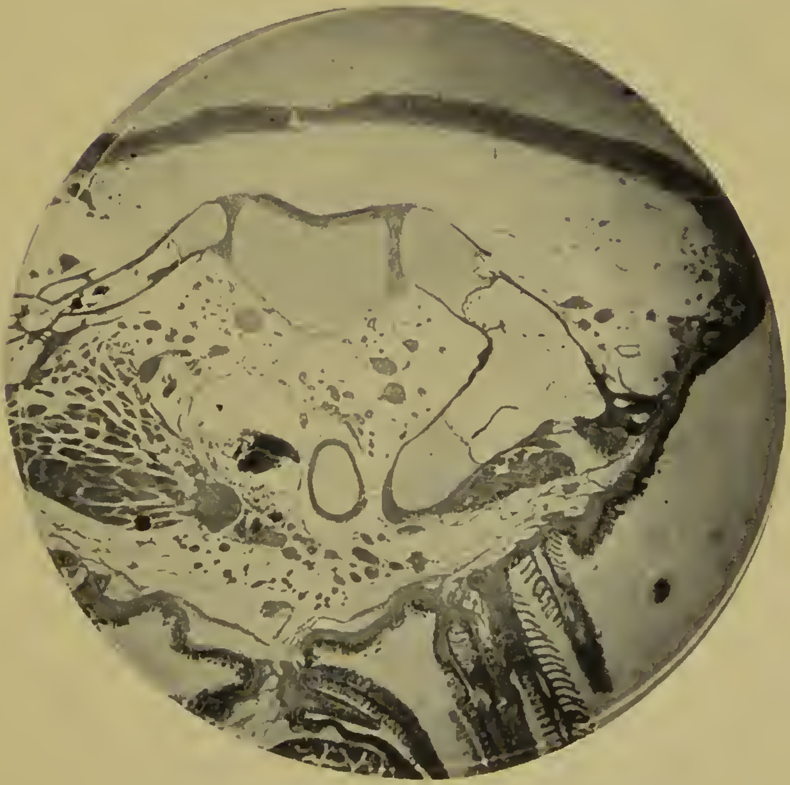

Fig. 9.

(Marine: Goitre in Brook Trout.

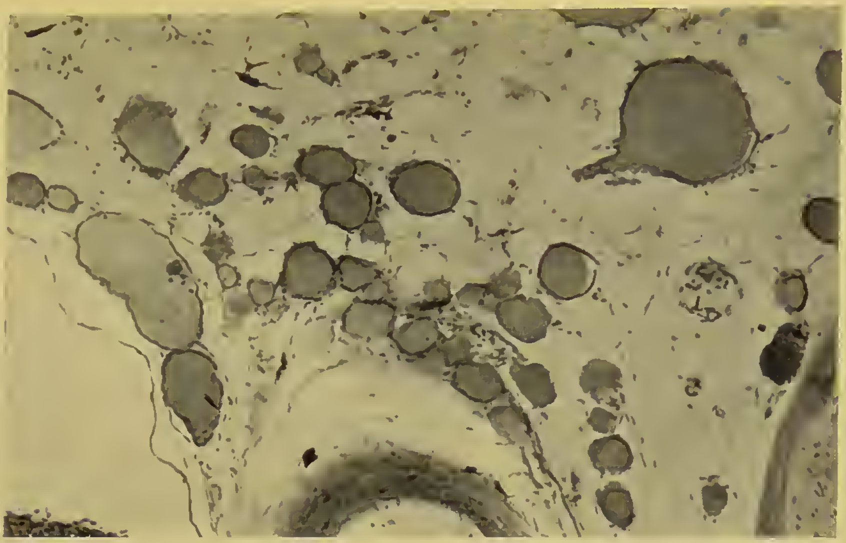

FIG. 10.

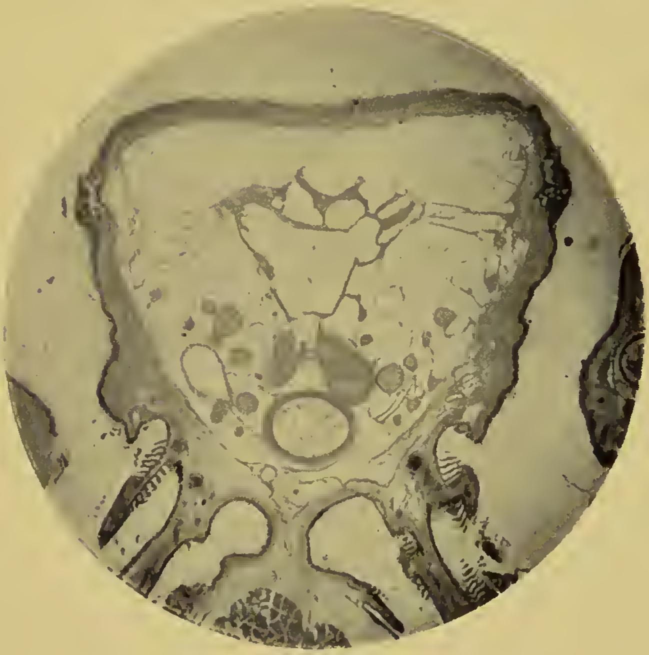

FIG. 11.

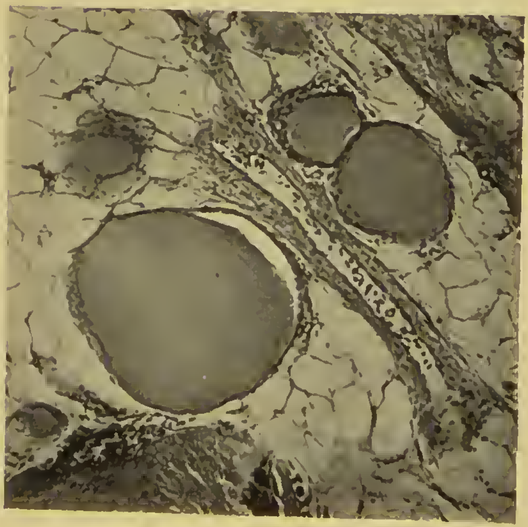

FIG. 12.

(Marine: Goitre in Brook Trout.)

THE RAPIDITY OF THE INVOLUTION OF ACTIVE THYROID HYPERPLASIAS OF BROOK TROUT FOLLOWING THE USE OF FRESH SEA FISH AS A FOOD.

TABLE I.

Pond No.	Age in months.	Date taken.	Food and length of time fed.	Condition of thyroid.		Remarks.
				Extent of overgrowth.	Classification.	
8	8+	Sept. 28, 1913	Hog's liver for 1st 4 mos. of life; then hog's liver and heart	Entire subpharyngeal area infiltrated, including bone and muscle	Marked hyperplasia	This is an example of 8 controls. All have approximately the same degree of hyperplasia.[3] Colloid absent.
8	8+	Oct. 5, 1913	Whole butter fish only, beginning Sept. 28, 1913, 1 wk.	Entire subpharyngeal area infiltrated, including bone and muscle	Colloid-moderate-marked hyperplasia (beginning involution)	This is an example of 4 specimens examined. All have approximately the same thyroid condition. Colloid appears in follicles.
8	8+	Oct. 12, 1913	Butter fish only for 2 wks.	Thyroid area filled, extending to pharyngeal mucosa, in bone and muscle	Colloid-moderate hyperplasia (involuting)	This is an example of 4 specimens examined. All have approximately the same thyroid condition. Colloid in fair amounts in all follicles. Epithelium low columnar.
8	9	Oct. 19, 1913	Butter fish only for 3 wks.	Entire subpharyngeal area filled, extending to pharyngeal mucosa and skin and gills, in bone and muscle	Colloid-early (involuting)	This is an example of 4 specimens examined. All have approximately the same thyroid condition. Colloid in all follicles fairly homogeneous. Epithelium cuboidal.
8	9+	Oct. 26, 1913	Butter fish only for 4 wks.	Entire subpharyngeal area filled, extending to pharyngeal mucosa, bone, and muscle	Colloid-early (approximating pure colloid)	This is an example of 4 specimens examined. All have approximately the same thyroid condition. Colloid dense, nearly uniform. Follicles more separate and stroma more prominent, due to shrinkage of blood supply and size of follicles. Epithelium cuboidal.

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[3] Complete examinations of all the fry at the hatchery were made in August, and all were found to have thyroid hyperplasia (Marine, D., *Jour. Exper. Med.*, 1914, xix, 70).

Pond No.	Age in months.	Date taken.	Food and length of time fed.	Condition of thyroid		Remarks.
				Extent of overgrowth.	Classification.	
8	9+	Nov. 2, 1913	Butter fish only for 5 wks.	Entire subpharyngeal area filled, extending to pharyngeal mucosa, to bone, muscle, and gills	Colloid goitre (complete involution)	This is an example of 4 specimens examined. All have approximately the same thyroid condition. Colloid dense, uniform. Follicles separate. Epithelium low cuboidal.
8	9+	Nov. 9, 1913	Butter fish only for 6 wks.	Entire subpharyngeal area filled, extending to pharynx mucosa, bone, and muscle	Colloid goitre (complete involution)	This is an example of 4 specimens examined, all showing same thyroid condition.
8	10	Nov. 16, 1913	Butter fish only for 7 wks.	Entire subpharyngeal area filled, extending to skin, pharyngeal mucosa, bone, and muscle	Colloid goitre (complete involution)	This is an example of 4 specimens examined, all showing same thyroid condition.
8	10+	Nov. 23, 1913	Butter fish only for 8 wks.	Entire subpharyngeal area filled, in bone and muscle	Colloid goitre (complete involution)	This is an example of 4 specimens examined, all showing same thyroid condition.
8	10+	Nov. 30, 1913	Butter fish only for 9 wks.	Entire thyroid area filled, extending to pharyngeal mucosa, to bone, and muscle	Colloid goitre (complete involution)	This is an example of 4 specimens, all showing same thyroid condition.

are still present at the colloid-epithelium junction. By the use of less rigid standards than I have adopted, these thyroids could be classified as completely involuted rather than as "colloid-early hyperplasias." By comparing the follicles with those of normal fish or with those seen in the subsequent specimens of this series, however, it is evident that the involution is not complete. The specimens taken after thirty-five days of fish feeding are listed as "complete involutions"; that is, the lining epithelium is low cuboidal. The stainable colloid is homogenous, and nearly uniform in all follicles. The follicles are smaller and more widely separated from each other, while the stroma is correspondingly more prominent. The capillaries about the follicles are less prominent. The distribution of the follicles is, of course, the same as that attained during the growing actively hyperplastic stage, *i. e.,* in bone and muscle with extension to the skin and pharyngeal mucosa.

The specimens examined on the 42d, 49th, 56th, and 63d days respectively are nearly identical with those of the 35th day. There is probably some further involution in the last specimens, as evidenced by a slight increase in the staining density of the colloid and in the flattening of the lining epithelium. This is also true of normal thyroid follicles, and has occasioned much discussion as to what is the normal type. In a tissue like the thyroid epithelium, which is capable of such marked hypertrophy and hyperplasia, as well as marked involution, one must adopt somewhat arbitrary groups, within which variations between certain narrow limits are not taken into account.

The time in which complete involution of these relatively mild degrees of thyroid hyperplasia occurs, following the use of butter fish in this particular environment and strain of brook trout, is about thirty-five days. As was shown in a previous paper (1), the thyroid gland, once involuted, remains in this colloid or involuted stage as long as the fish are fed with this food. No further growth of the thyroid takes place under these conditions. Thus the thyroids of the three and two year old brook trout at this hatchery have the same amount of thyroid tissue with the same distribution of follicles that was attained during the first ten months of their lives, at which time the change of food was instituted.

Iodin involutes the hyperplasias more rapidly than butter fish. In Lake Erie pike with mild degrees of thyroid hyperplasia it was found (2) that iodin involuted them in from sixteen to eighteen days.

In the experiments of 1909 (3) it was found that the thyroid of twenty months old brook trout with extensive hyperplasia involuted in from twenty to twenty-five days following the daily addition of traces of iodin to the water. In the iodin experiments of 1910 (4) it was found that involution took place in about forty days in twenty-nine months old brook trout with large and often slightly ulcerated goitres, while in forty-one months old emaciated brook trout with extensively infected and ulcerated external goitres healing and involution were complete at the sixty-second day. In mammals the involution with iodin is of course more rapid (5). In young dogs with uncomplicated simple hyperplasias, the involution is usually complete in from fourteen to eighteen days.

As the whole butter fish contains appreciable amounts of iodin[4] one may ask whether this effect of fish as food is merely the well known iodin action, and the somewhat longer involution time only the manifestation of a very dilute solution. In the absence of any data against this view, I prefer tentatively to consider it an iodin effect rather than to postulate another explanation in favor of which there are at present no direct data. Experiments are now in progress which it is hoped will shed some light on this question.

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[4] Iodin in fish, birds, and mammals is, for the most part, contained in the thyroid glands, although traces of iodin have been found in certain fish oils, as, for example, cod liver oil, where presumably contamination with thyroid was avoided. Using the modified Baumann and the Hunter methods, I have not been able to recognize traces of iodin in whole amphioxus and in butter fish (*Stromateus triacanthus*) and weak fish (*Cynoscion regalis*) from which the thyroid areas had been removed. A. T. Cameron (*Biochem. Jour.*, 1913, vii, 466; *Jour. Biol. Chem.*, 1914, xvi, 465) has published the finding of relatively large amounts of iodin in the thyroids of rays and dog fish. Thus in *Raia clavata* he found the mean iodin content to be 0.438 per cent. of dried gland, while in *Scyllium canicula* he found a mean content of 1.16 per cent. of dried gland. I have made the following iodin estimations in butter fish:

(1) With whole butter fish in 1 gm. amounts = possible trace.
(2) With whole butter fish in 5 gm. amounts = trace, unmeasurable.
(3) With butter fish, exclusive of the thyroid area, in 1 gm amounts = no trace.
(4) With butter fish, exclusive of the thyroid area, in 5 gm. amounts = no trace.

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73 (890)

Parathyroid hypertrophy and hyperplasia in fowls.

By **David Marine** (*by invitation*).

[*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland, Ohio.*]

Physiological overgrowth of the parathyroid glands in mammals has been very rarely observed. Erdheim,[1] Bauer[2] and Strada[3] have recently described its occurrence in man in association with some cases of osteomalacia. Three instances of undoubted general parathyroid enlargement in bitches in association with lactation have come under my observation.

In the reports of partial removal and of transplantation of mammalian parathyroids, particularly in dogs, one of the most characteristic features has been the absence of any noteworthy compensatory enlargement of the remaining portion within the time limits in which other tissues, like the thyroid, heart muscle, kidney, etc., react to artificially induced insufficiencies.

In the course of some experiments with the thyroid gland in fowls in 1910, I observed several instances of marked enlargement of the parathyroids independent of the changes occurring in the thyroid glands. These parathyroid changes were found in fowls which had been fed with maize and wheat for periods of 2 to 6 months. The observations were repeated in 1911, 1912, and 1913, with similar results.

Since calcium temporarily relieves the symptoms of parathyroid tetany in mammals, and since maize and wheat contain very little calcium, it was thought possibly the parathyroid overgrowth might be a result of a calcium deficiency, and if this was so, calcium might exert some protective action against parathyroid overgrowth.

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[1] Erdheim, J., "Ueber Epithelkörperbefunde bei Osteomalacie," *Sitz. Ber. Akad. Wiss.*, 1907, Bd. CXVI, 311–370.

[2] Bauer, T., "Morphologische Studien über die Beziehungen der Epithelkörperchen zum Kalkstoffwechsel," *Frankfurt. Zeitschr. f. Path.*, 1911, VII, 23.

[3] Strada, F., "Le paratiroide nell' osteomalacia e nell' osteoporosi senile," *Pathologica Anno*, I, 1909, 423–437.

Calcium hydroxide, calcium lactate, calcium carbonate (as chalk and crushed oyster shells), magnesium carbonate, strontium carbonate, sodium citrate, sulphuric acid, neutral sulphur and sodium hydroxide have been given in the diet of maize and wheat for periods of one, two and three months. One hundred and ten fowls have been used. No detectable inhibition of the parathyroid overgrowth could be detected in the fowls given magnesium carbonate, strontium carbonate, sulphuric acid, neutral sulphur, sodium citrate or sodium hydroxide,—the growth being as marked as in the controls. On the other hand, those given sulphuric acid and neutral sulphur had more marked parathyroid enlargements and softening of the bones than those given the other chemical substances or the controls. In those fowls which had received calcium there was uniformly less parathyroid overgrowth; in those given calcium hydroxide and calcium carbonate it was barely detectable; while in those given calcium lactate there was moderate enlargement. No differences ascribable to sex could be determined.

These observations suggest: (*a*) that the parathyroids of birds are more susceptible to overgrowth than those of mammals; (*b*) that calcium offers some protection against overgrowth; and (*c*) that the parathyroids (as MacCallum has suggested) are intimately associated with the function of calcium in the complex of body metabolism and nutrition.

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36 (853)

Blood platelets and blood clotting.

By **T. F. Zucker** (by invitation).

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That the formed elements of the blood play a part in normal coagulation has long been known. Both leucocytes and platelets have been said to yield substances which contribute to fibrin formation. Leucocytes alone, however, will not coagulate fibrinogen. Cramer and Pringle[1] have recently shown that oxalate plasma freed from platelets by filtering through clay filters does not clot on adding an amount of $CaCl_2$ which causes a similar centrifuged but unfiltered plasma to clot in a short time. That platelets disintegrate during coagulation, and that the addition of oxalate preserved them is well known. As early as 1881 Fano[2] appreciated the fact that centrifuging was not sufficient to remove all cellular elements, and therefore resorted to filtration through a clay filter.

Regarding the effect of other anticoagulants, it has been observed by Buerker[3] and by Deetjen[4] that the breaking down of platelets in shed blood as observed under the microscope was inhibited by all those substances which can be used in preventing coagulation. They mention oxalates, citrates, NaPO, Na_2HPO_{43}, salts of Mn, Fe and Ni, $MgSO_4$, Na_2CO_3, peroxides and hirudin. The fact that these substances all have platelet preservative properties, does not necessarily mean that their anticoagulant effect is due solely to the fact that platelets remain intact.

The experiments of Cramer and Pringle seem to show that oxalate is an anticoagulant because it preserves platelets. That this is more generally the mode of action of anticoagulants is shown by the following data. Citrate plasma gives exactly the same results as oxalate plasma, which has also been verified by others. Of greater interest than citrate are the anticoagulants which do not affect calcium. A plasma was obtained by drawing blood into an equal volume of a 1 per cent. solution of $MnCl_2$ in 0.9 per cent. NaCl. If this is treated with enough Na_2HPO_4 to precipitate the manganese, it coagulates quite readily. On centrifuging this plasma at a moderate speed to remove red cells and leucocytes (this also throws down some platelets), the coagulation is slightly deferred. By filtering through a clay filter a plasma is obtained which is not coagulated at all by Na_2HPO_4. Further evidence is furnished by making use of the fact that platelets on disintegrating yield a vasoconstrictor material.[1] The manganese chloride plasma when tested on artery rings gives no constriction, but on addition of Na_2HPO_4 it clots and gives marked constriction. This is the same result obtained with citrate and $CaCl_2$, and indicates clearly that the change taking place on adding Na_2HPO_4 is disintegration of platelets.

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[1] *Quart. Journ. Exp. Physiol.*, 6, 1 (1913).

[2] *Arch. f. Physiol.*, 1881, p. 277.

[3] Buerker, *Pflug. Arch.*, 102, 36 (1904).

[4] Deetjen, *Zts. physiol. Chem.*, 63, 1 (1909).

The observation of Buerker that $MgSO_4$ preserves platelets I have verified by centrifuging a magnesium sulphate plasma fractionally and staining the sediment with Wright's stain. The same was observed with NaCl and Na_2SO_4. It is, however, much more difficult to separate platelets from plasmas containing high concentration of salts (NaCl, $MgSO_4$, Na_2SO_4) than with oxalate citrate or fluoride, one reason being that on centrifuging the leucocytes and platelets do not form a well-marked zone, but largely sink into the red cell layer.

If a fresh salted plasma (I have used $MgSO_4$ and NaCl) is thoroughly centrifuged to remove the platelets as far as possible, this plasma when compared with the cell containing residue after dilution of both with normal saline, shows a much greater clotting time, or does not clot at all. The high concentration of salts does not permit the use of the test for vasoconstrictor material.

Hirudin also as tested by Buerker's or Deetjen's method preserves platelets. O'Connor[2] and others have found that hirudin prevents the liberation of vasoconstrictor material in shed blood. This indicates that hirudin prevents coagulation not only by an antithrombin action, but also by preserving platelets. Which of these plays the more important rôle in keeping blood in a fluid state cannot as yet be definitely decided. It seems to follow from the results stated above that if hirudin is used in sufficient quantity to prevent platelet disintegration entirely, the antithrombin action will not come into play at all.

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[1] Zucker and Stewart, *Zentr. f. Physiol.*, 27, 85 (1913).

[2] *Arch. f. Exp. Path. and Pharmakol.*, 67, 195 (1912).

Concerning the physico-chemical mechanism of platelet disintegration, we can as yet say nothing definite. Ca ions seem to be essential, and on that basis the effect of calcium precipitants (oxalates and fluorides) can be explained. Whether citrate decreases the ionization of Ca sufficiently to make the remaining Ca ions negligible has, I believe, never been determined quantitatively. Mn salts do not affect the calcium, but act directly on the platelets, and the possibility suggests itself that the action of citrates may be of the same kind. Gessard[1] reports data which show an antagonism between Ca and Mn ions, *i. e.*, within certain limits additional calcium may overcome the anticoagulant effect of Mn. Regarding the mode of action of hirudin and salts used in "salted plasmas," nothing at all can be said.

To decide the question whether the platelet preservatives antagonize the disturbing action of calcium on colloidal equilibrium of the lipoids of the cell membrane (*i. e.*, surface layer) as recently suggested by Clowes[2] and West for citrate, would require further experiments.

The suggestion of Buerker that clotting is the immediate consequence of platelet disintegration acquires new interest in the light of the experiments with clay filters. It will be noticed that the material to which the name prothrombin has been given closely corresponds in properties to intact platelets. In that case thrombin would be equivalent to disintegrated platelets; thrombokinase would be any substance ($CaCl_2$, tissue juices) which accelerates the disintegration of platelets.

From the above data, it appears clearly that the condition of platelets is of the greatest importance in coagulation. We cannot say that preserving the platelets intact is the only means of keeping blood in a fluid condition, but it does seem that in every case where blood remains uncoagulated, the platelets are involved in some way. Experiments now in progress on the part which platelets play in the formation of peptone plasma are reserved for a separate communication. It may be stated here that after injection of peptone into a dog, the platelets are not destroyed (a statement often met with), although they disappear from circulating blood, and that in the blood there appears a substance similar in its actions to hirudin, which preserves platelets and prevents formation of fibrin (antithrombin).

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[1] *Compt. Rend.*, 153, 1241 (1911).

[2] PROC. SOC. EXP. BIOL. AND MED., XI, 6, 1913.

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COMPLEMENT DEVIATION BY CORPUS LUTEAN ANTIGENS.

BY

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THE fact that the ovary fulfils two functions—one of ovulation and one of trophic or nutritional activity—has been fairly well established. We now know that the ovary possesses a powerful influence over the nervous system of the individual, over the development of the uterus and of the breasts, and over the phenomenon of menstruation.

That such properties of the ovary reside chiefly if not entirely in the corpora lutea is strongly indicated by such facts as the following: 1. In experiments in which the ovary has been transplanted to an animal previously deprived of its own ovaries, no trophic results from the transplantation are seen unless the new ovary survives in such a condition that ovulation takes place—*i.e.*, an ovum is discharged and a corpus luteum is formed. 2. The destruction of the corpus luteum in the ovary of a pregnant rabbit prevents the complete development of the pregnant uterus and its contained ovum. 3. The destruction of the corpus luteum in a nonpregnant female causes the next menstruation to be missed.*

Furthermore, it seems to be established that the corpus luteum acts through the medium of some internal secretion; for a reflex action through the nerves is disproved by the fact that a transplanted ovary containing lutean tissue will act almost as well as an ovary whose nerve connections are intact.†

The term "internal secretion" does not necessarily, nor indeed usually imply a substance of such a nature as would produce an antibody; and we have, of course, no right to postulate any such idea as a fact. We may, however, use the term merely as a convenient expression for an unknown quantity. The idea has suggested itself that if the ovary has such an internal secretion, an antibody may be generated in the blood serum of the woman. If so, might it not be possible to detect this antibody by a complement deviation test, using as the antigen an extract of corpus lutean tissue?

Dr. J. W. Miller,‡ working in Dr. Wassermann's laboratory, has experimented by immunizing dogs, rabbits, etc., with repeated

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* Fraenkel. *Arch. f. Gyn.*, 1910, xci, 705.
† Knauer. *Arch. f. Gyn.*, vol. lx, 1900.
‡ *Cent. f. Bakt.*, vol. xlvi, p. 639.

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injections of fresh corpus lutean tissue from cows and sows. Later, the serum of the injected animals, in combination with an antigen prepared from corpora lutea, will deviate complement. In Dr. Miller's paper the suggestion is thrown out that pregnancy might be diagnosed by some such test, the corpus luteum of pregnancy being so large.

To test this tneory, a number of antigens have been prepared in different ways, and tested with serum from the blood of patients in the Lakeside Hospital, Cleveland. All the corpora lutea used were obtained fresh at operations in the clinic of Dr. Hunter Robb, to whom I wish to express my gratitude, not only for the use of the material, but also for his interest. The blood of the patients from whom the corpora lutea were removed was tested in almost every case by the Wassermann reaction for lues. In like manner, tests for syphilis were made upon the blood of those patients whose serum was used. These women were mostly young, and about half of them were pregnant. Serum from the blood of males was generally used as a control.

The antigen was prepared in one of three ways. What we have termed antigen A and antigen B in the subjoined tabulation of our results were obtained by following Noguchi's technic in preparing the pure lipoids, as described by him in "The Serum Diagnosis of Syphilis."* This pure lipoid was so diluted that 0.1 c.c. of a 0.6 per-cent. and the same amount of a 1.2 per-cent. solution could be used in the tests. The antigen designated A2 was prepared according to the technic described by Dr. Miller in the article mentioned above. The corpus lutean tissue was chopped fine and placed in a normal saline solution containing 0.5 per cent. phenol. Three cubic centimeters of the fluid were used for each gram of substance. The emulsion was thoroughly shaken and the clear fluid decanted after standing. This was centrifuged till quite clear. The antigens termed C and D were simple alcoholic extracts of corpora lutea, the tissue being chopped fine and then extracted with ten volumes by weight of absolute alcohol for a period of a week, the flask being placed in the incubator. This technic was also used with the sheep's ovaries, which were extracted and tested with sheep's blood serum.

Through the great kindness of Drs. Dexter and Cummer, I was permitted to set up the complement fixation tests with the use of their hemolysin, guinea-pig complement, washed sheep's erythrocytes, etc. My thanks are especially due to them. The technic of this part of the work was that described by Swift.†

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* J B. Lippincott Co., Phila., 2nd Ed.

† International Clinics, Series 20, No. 1.

The great difficulty in obtaining enough fresh corpus lutean tissue for making the antigens has been the chief trouble encountered in these experiments. For example, in the cases of antigens A and B, barely enough lipoid could be obtained from the single corpus luteum on hand to permit of the testing of a very few blood sera. The series of cases we have summarized in the accompanying table is, accordingly, quite small; and it is only the fact that our results have been negative that has led us to consider them of any value.

The blood sera of twelve women have been tested; and in addition that of ten male controls. Blood of male and female sheep has also been tested. There was complete hemolysis with both the sheep sera. In all these tests, a distinct complement deviation was noted seven times—four times with female sera and three times with that of male controls. Using Swift's scheme for denoting the degree of the fixation, we find:

	Male	Female
+++	2	1
++	1	0
+	0	2
+−	0	1

It is especially interesting to note that five sera gave a definite Wassermann test for syphilis—two female and three male. Every one of these syphilitic sera, whether male or female, showed a complement fixation with antigen made from corpus lutean tissue. The only other complement deviations observed in the series occurred very indefinitely, one being rated a (+) and the other only a (+−). As no Wassermann test was done upon the second of these, we cannot say whether or not the patient was syphilitic. One known luetic serum, from a male, showed complement deviation with one corpus lutean antigen, but complete hemolysis with another; and the same contradictory result was obtained with serum from one of the female patients. Antigen B was prepared from the corpus luteum of a patient whose blood gave a positive Wassermann test, and this fact may account for the (+) reaction mentioned above with the only serum tested with this antigen.

As it was impossible to find anything against which to standardize the antigens, the dilutions used had to be more or less empirical. The alcoholic antigens (C and D) were made up with 2, 3, 5, and 6 parts of normal salt solution. In each case, 0.5 c.c. of the mixture was used in a test.

CONCLUSIONS FROM THE SERIES OF TWENTY-FOUR EXPERIMENTS.

1. Attempts to detect the "internal secretion" of the corpus luteum by a complement deviation test, using extract of corpus luteum as an antigen, have proved negative.

2. An antigen prepared by extracting corpus luteum will deviate complement with the blood serum of patients giving the Wassermann test for syphilis.

ANTIGENS.

Pure lipoids.......... { A from one normal corpus luteum.
{ B from one luetic corpus luteum.
Watery extract..........A2 from one normal corpus luteum.
Alcoholic extract...... { C from six normal corpora lutea.
{ D from two normal corpora lutea.

Patient	Age	Wassermann	A		A2	B	C			D			Alc. ext. sheep's ovaries	
			0.6%	1.2%		1.2%	1–2	1–3	1–6	1–2	1–3	1–5	1–2	1–4
1	21	–		+										
2	52	+++		–		+								
Male control.		–		–		–								
3	40	+++	+++	+										
Male control.		++	+++	+										
4	22	–			–									
5	33	–										–		
Male control.		–										–		
6	23	?								±				
7	36	–									–			
Male control.		?									–			
8 (preg.)	28	–									–			
9 (preg.)	22	–						–	–					
Male control.		–						–	–					
10 (preg.)	36	–						–						
Male control.		–						–						
11 (preg.)	30	–					–			–				
Male control.		–					–			–				
Luetic male control.		+++					+++			+++				
12 (preg.)	37	–					–			–				
Male control.		–					–			–				
Luetic male control.		+++					++			–				
Sheeps serum { male													–	–
Sheeps serum { female													–	–

628 ROSE BUILDING.

FURTHER OBSERVATIONS ON THE RELATION OF IODIN TO THE STRUCTURE OF THE THYROID GLAND IN THE SHEEP, DOG, HOG AND OX *

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INTRODUCTION

In this report we have collected our observations on the relation of the iodin content to the structure of the thyroid to include sheep, ox and hog thyroids. It is thus only a continuation of the work previously reported[1] concerning dogs' thyroids. The methods used and the anatomic classifications adopted are the same as those fully described in the above-mentioned article and elsewhere.[2]

COMPARISON OF THE IODIN CONTENTS OF SHEEP, DOG, HOG AND OX THYROIDS WITH THEIR RESPECTIVE ANATOMIC STRUCTURES

The following tables are compiled from iodin determinations made on the thyroids of 40 sheep, 67 dogs, 26 hogs and 37 oxen. As the basis of these tables we have used nine anatomic groups, viz.:

1. Normal glands.
2. Colloid glands (goiters).
3. Colloid-early glandular hyperplasia.
4. Normal-early glandular hyperplasia.
5. Early-glandular hyperplasia.
6. Early-moderate glandular hyperplasia.
7. Moderate glandular hyperplasia.
8. Moderate-marked glandular hyperplasia.
9. Marked glandular hyperplasia.

The normal and colloid groups are well defined, while the remaining seven groups are purely arbitrary divisions of the hyperplasias made for the purpose of facilitating analysis, since in reality one has to deal with a continuous gradation of hyperplastic changes occurring in either normal or colloid glands. In order to express this gradation, we have used the following terms: *normal-early glandular hyperplasia* to include those glands showing the very earliest hyperplastic changes occurring in normal glands; *colloid-early glandular hyperplasia* to include glands showing the earliest hyperplastic changes occurring in colloid glands, and the terms *early, moderate, marked,* etc., to include the other gradations up to and including the most extensive glandular hyperplasias met with.

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* From the Laboratories of Experimental Medicine and Pharmacology, Western Reserve University.

[1] Marine (David) and Williams (W. W.): THE ARCHIVES INT. MED., 1908, i, 349.

[2] Marine (David): The occurrence and physiological nature of glandular hyperplasia, etc. Johns Hopkins Hosp. Bull., 1907, xviii, 359.

In placing these glands in these several anatomic groups, we have compared all the glands of the four animals, the one with the other, in order that the same standard of classification might obtain in all.

In each of the following tables we have listed for comparison the iodin contents of sheep, dog, hog and ox thyroids having the same anatomic structure.

TABLE 1.—NORMAL GLANDS *

Animal.	No. Cases.	Iodin per gm. dried.			Iodin per gm. fresh.		
		E.	M.	A.	E.	M.	A.
Sheep	19	4.614 1.247	2.288	2.467	1.318 0.318	0.694	0.686
Dog	3	4.722 1.990	3.205	3.322	1.064 0.512	0.757	0.777
Hog	18	4.153 1.538	2.412	2.515	1.456 0.425	0.778	0.884
Ox	17	4.768 2.730	3.254	3.461	1.592 0.892	1.069	1.117

* In each table E., M., A. are abbreviations for extreme, mean and average, respectively.

It will be seen that the upper extremes of iodin contents are fairly constant for all four animals, while the lower extremes show moderately wide variations, although the lowest of these lower extremes is always far in excess of the highest extremes of the succeeding group—normal-early glandular hyperplasias. This would indicate that there are considerable variations in the iodin contents within the group, even when no noteworthy anatomic changes are observed, although if individual comparisons of the iodin contents with the corresponding histologic preparations be made one can distinguish changes in the structure (too slight to warrant the introduction of a new group) corresponding to the variations in the iodin content; that is, glands with the highest iodin contents have a more flattened alveolar epithelium and *vice versa,* although all these glands appear in the table as normal.

The average iodin contents for the four animals show a surprising constancy and parallelism, viz.: 2.467 mg. for the sheep, 2.515 for the hog, 3.322 for the dog and 3.461 for the ox per gm. of dried thyroid

The ox thyroids in our series have distinctly higher iodin contents than either the dog, sheep or hog. To know whether this is normally true would be of value in determining what relation exists between the normal iodin content and the normal weight of the thyroid, since oxen appear to have less thyroid per kilogram of body weight than do the other animals mentioned. From the experimental side it has been definitely shown that the amount of iodin in the thyroid does to a great extent control the size of the gland.

TABLE 2.—COLLOID GLANDS

Animal.	No. Cases.	Iodin per gm. dried.			Iodin per gm. fresh.		
		E.	M.	A.	E.	M.	A.
Sheep	3	3.691 1.769	3.529	2.996	1.027 0.455	0.974	0.818
Dog	8	3.608 0.846	1.816	1.985	1.039 0.132	0.406	0.459
Hog	2	2.768 1.938	.....	2.353	0.805 0.557	.....	0.681
Ox	0	.....	.....	.....	.....	.....	.....

Owing to the small number of cases included, it is not possible to speak very specifically. However, in all three animals in which colloids were observed the upper extremes of iodin content are fairly constant, while the lower extremes show moderate variations. This agrees with what was observed in the normal glands, and our explanation is the same. Another point worthy of note is that, while the iodin per gram of colloid gland is in general lower than that of normal glands, yet, as will be seen, they approach nearest to the normal iodin content so far as we have found and may be raised to an equal content with the normal glands.

TABLE 3.—COLLOID-EARLY GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried.			Iodin per gm. fresh.		
		E.	M.	A.	E.	M.	A.
Sheep	4	1.000 0.461	0.853	0.792	0.282 0.138	0.201	0.206
Dog	4	1.443 0.431	0.953	0.945	0.302 0.125	0.221	0.217
Hog	0	.....	.....	.....	.....	.....	.....
Ox	0	.....	.....	.....	.....	.....	.....

Table 3 and Table 4 deal with the most important anatomic and chemical changes concerned with the production of goiter, in that they represent the first deviation or change from the normal-colloid or quiescent glands. *Colloid-early glandular hyperplasias* differ from *normal-early glandular hyperplasias* in that the former are *secondary*[3] hyperplasias, while the latter are *primary.* It is to be regretted that more colloid-early glands were not obtainable (the probable reason for this will be pointed out later). The extremes show a fair constancy. In the sheep the highest extreme iodin content is below the lowest pure colloid extreme. In the case of the dog this is in general true, though there are exceptions which we are not able to explain. The existence of these exceptions suggests, however, that from the histology alone one is unable to say whether a given gland is undergoing further hyperplasia from a less marked hyperplasia or *vice versa.* The averages also are constant and in every instance show the great drop in the percentage of iodin from that of pure colloid glands. This drop is, as will be seen in Table 4, identical with that occurring between the normal and normal-early glandular hyperplasia. Between no other groups are there comparable drops. This means that in both colloid and normal glands there are wide variations in the amount of iodin present, but that there is a quite constant lower limit of the iodin content necessary to maintain normal gland or pure colloid gland structure, and that this lower limit for colloids is slightly in excess of 0.217 mg. per gram of fresh thyroid for dogs and 0.206 mg. per gram of fresh gland for sheep, corresponding to 0.792 mg. and 0.945 mg. per gram of dried gland, respectively.

TABLE 4.—NORMAL-EARLY GLANDULAR HYPERPLASIA

	No.	Iodin per gm. dried.			Iodin per gm. fresh.		
Animal.	Cases.	E.	M.	A.	E.	M.	A.
Sheep	1	.....	.....	0.677	.....	.....	0.176
Dog	7	1.296 0.483	0.815	0.879	0.318 0.018	0.153	0.174
Hog	1	.....	.....	1.230	.....	.....	0.337
Ox	7	2.676 2.000	2.307	2.317	0.726 0.482	0.653	0.628

Table 4, together with Table 3, deals with the most important thyroid changes concerned in the production of goiter. It is seen that the highest extremes of iodin content are invariably below the lowest extreme iodin contents of normal glands. This is even more evident with the means and averages. The table also shows that there is considerable difference between the average iodin content of sheep's thyroids and that of oxen thyroids, just as was seen to be true of the normal glands of these animals. It suggests, as was stated under Table 1, that oxen normally have more iodin and less thyroid per kilogram of body weight. In accordance with this, hyperplastic changes are manifest with an iodin content nearly four times that of the sheep's thyroids. But the most striking thing, just as in the colloid-early glands, is the great drop in iodin content from the normal, which must occur before hyperplastic changes are observed. The table shows that the lower limit of iodin necessary for the maintenance of normal structure is somewhat in excess of 0.176 mg. per gram of fresh gland for sheep, 0.174 for dogs, 0.337 for hogs and 0.628 for cattle, or 0.677, 0.879, 1.230, 2.317 mg. per gram of dried gland, respectively.

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[3] Secondary in the sense that this is the second time these glands have undergone active hyperplasia.

TABLE 5.—EARLY GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried. E.	M.	A.	Iodin per gm. fresh. E.	M.	A.
Sheep	0	.....	.....	.....	.....	.....	.....
Dog	9	1.028 0.243	0.654	0.625	0.235 0.063	0.113	0.139
Hog	2	1.158 1.046	.....	1.102	0.291 0.279	....	0.285
Ox	3	2.186 1.123	1.630	1.646	0.615 0.314	0.456	0.462

In the group of early glandular hyperplasia the iodin contents are still further lowered and the drop is practically the same in all four animals. The ox thyroids still show higher iodin contents than the other animals' glands for the same degree of thyroid hyperplasia as was also noted in the normal and normal-early glands.

TABLE 6.—EARLY-MODERATE GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried. E.	M.	A.	Iodin per gm. fresh. E.	M.	A.
Sheep	1	.....	.....	0.548	.....	.....	0.131
Dog	1	.....	.....	0.262	.....	.....	0.082
Hog	3	0.846 0.769	0.769	0.795	0.241 0.198	0.233	0.224
Ox	5	1.030 0.969	1.000	1.000	0.252 0.205	0.222	0.226

In the table of early-moderate glandular hyperplasia are collected those glands which histologically show a degree of epithelial proliferation (hyperplasia) too pronounced to be considered as early glandular hyperplasia and not sufficient to be classed as moderate glandular hyperplasia. As regards their iodin contents, the upper extremes are in every instance lower than the lower extremes of the preceding group (early glandular hyperplasia). So also the average iodin contents are about as much below those of the group of early glandular hyperplasias as the early glandular hyperplasias are below the group of normal-early glandular hyperplasias.

TABLE 7.—MODERATE GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried.			Iodin per gm. fresh.		
		E.	M.	A.	E.	M.	A.
Sheep	1	.....	.....	0.400	.....	.....	0.091
Dog	9	0.854 0.101	0.345	0.368	0.136 0.026	0.076	0.078
Hog	0	.....	.....	.....	.....	.....	.....
Ox	0	.....	.....	.....	.....	.....	.....

There being no glands from hogs or oxen and but one from the sheep series that histologically belonged to the group of moderate glandular hyperplasia, comparisons are impossible. The average iodin contents of the cases recorded are as usual below those of the preceding group.

TABLE 8.—MODERATE-MARKED GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried.			Iodin per gm. fresh.		
		E.	M.	A.	E.	M.	A.
Sheep	5	0.092 0.000	0.024	0.031	0.014 0.000	0.003	0.004
Dog	9	0.660 0.058	0.231	0.283	0.109 0.011	0.042	0.055
Hog	0	.....	.....	.....	.....	.....	.....
Ox	0	.....	.....	.....	.....	.....	.....

In the group of moderate-marked hyperplasia also there are but two animals represented. The extremes of iodin content in the dog thyroids are widely separated. As has already been pointed out, it is impossible to tell from the histology alone whether a given gland is undergoing further hyperplasia or is reverting to a lesser degree, in which latter event the iodin would be higher. Another factor must also be considered, that is, that dogs live under far less constant conditions than sheep and oxen. It will be shown later that the more constant the conditions of life the more constant are the iodin contents. The averages show the same drop in the iodin contents proportional to the degree of increase of the hyperplasia.

TABLE 9.—MARKED GLANDULAR HYPERPLASIA

Animal.	No. Cases.	Iodin per gm. dried. E.	M.	A.	Iodin per gm. fresh. E.	M.	A.
Sheep	6	0.036 0.000	0.000	0.006	0.006 0.000	0.000	0.001
Dog	18	0.640 0.008	0.073	0.114	0.123 0.002	0.014	0.023
Hog	0	.....	.....	.....	.....	.....	.....
Ox	5	0.270 0.077	0.215	0.189	0.062 0.016	0.042	0.041

Table 9 includes those glands having the most marked degree of thyroid hyperplasia and in consequence the lowest iodin contents. The only glands in which no estimable amount of iodin was found were in sheep, although, histologically, the degree of hyperplasia was no greater than in other glands which showed traces of iodin. The average iodin contents are all lower than the averages of the preceding group. So also the extremes are lower except in dogs' thyroids, in which the same wide variations are noted as in Table 8. Our explanation is the same.

SUMMARY AND DISCUSSION

Table 10, showing average iodin contents, has been introduced both as a summary and to emphasize the relation which exists between the iodin contents and the corresponding histologic structure.

TABLE 10.—AVERAGES

Anatomic Groups.	Sheep. Iodin per gm. Dried.	Fresh.	Dog. Iodin per gm. Dried.	Fresh.	Hog. Iodin per gm. Dried.	Fresh.	Ox. Iodin per gm. Dried.	Fresh.
Normal	2.467	0.686	3.322	0.777	2.515	0.884	3.461	1.117
Normal-early	0.677	0.176	0.879	0.174	1.230	0.337	2.317	0.628
Early	.....	.....	0.625	0.139	1.102	0.285	1.646	0.462
Early-moderate ..	0.548	0.131	0.262	0.082	0.795	0.224	1.000	0.226
Moderate	0.400	0.091	0.368	0.078	.....	.....	.....	.....
Moderate-marked.	0.031	0.004	0.283	0.055	.....	.....	.....	.....
Marked	0.006	0.001	0.114	0.023	.....	.....	0.189	0.041
Colloid	2.996	0.818	1.985	0.459	2.353	0.681	.....	.....
Colloid-early	0.792	0.206	0.945	0.217	.....	.....	.....	.....

Since colloid glands differ from normal glands essentially in that they have undergone active hyperplasia, two series (1), normal, and (2), colloid, must be recognized. Taking up the normal series, which is practically complete in that it contains all the gradations of hyperplasia, it is seen that in all four species of animals the strictly normal glands have the highest iodin contents and those with marked glandular hyperplasia the lowest. The intervening groups show progressive decline, depending on the extent of the hyperplasia. The greatest drop in iodin content between any two successive groups occurs between the normal and the normal-early glandular hyperplasias, that is, those glands showing the earliest histologic deviation from normal. This great drop occurs with all four species and is similar in nature to the drop which occurs between the pure colloid glands and the colloid-early glandular hyperplasias. As has been said, this drop suggests that there is a minimum iodin content necessary for the maintenance of the normal or colloid state of the gland, and, since the amount of iodin present in normal or colloid glands is, as a rule, far in excess of this minimum, it is possible that this difference represents the reserve or factor of safety.

Certain details of this relation of iodin to the structure of the glands are more clearly shown in the full Tables 11, 12 and 13. Here it will be seen that by arranging the iodin contents in series from minimum to maximum, the glands are also arranged in series according to their histology, their colloid contents and their weights. In other words, the weights of the glands vary directly with the degree of hyperplasia and inversely with the percentage iodin content; the stainable colloid varies inversely with the degree of hyperplasia and directly with the iodin content, and the degree of hyperplasia varies inversely with the iodin contents (the normal and colloid series being, of course, considered separately).

It is also noticed that within any anatomic group there is considerable variation in the iodin contents. This is for the greater part due to the arbitrary anatomic groups, since the glands show histologic variations corresponding to the iodin variations, but not sufficient to warrant separate grouping. In other words, the arbitrary groups but imperfectly represent the gradations which the complete tables fully picture.

It may also be added that no special stress is laid on the actual figures of the iodin determinations, but only their relative importance as a series has been considered. Other observers with other methods may obtain different figures, but the relation between the iodin content and the gland structures, we believe, will always be found constant.

Passing now to the colloid series, it will be seen that only two groups of colloid glands have been observed: (1) pure colloids, (2) colloid-early glandular hyperplasia. This is noteworthy because in our human collection (to be reported), using the same anatomic classification and

TABLE 11.—PIGS' THYROIDS

Case No.	Age. Sex.	Condition.	Locality.	Weight of Gland.	Color.	Consistency.	Colloid.	Normal.	Colloid.	Normal-Early.	Colloid-Early.	Early.	Early-Moderate.	Moderate.	Moderate-Marked.	Marked.	Iodin per gm. Dried.	Iodin per gm. Fresh.
P. 2.	10 mos. M.*	Good	Iowa	?	Fleshy red	Moderately soft.	Reduced.	..	..	..	..	..	+	..	..	..	0.769	0.198
P. 24.	10 mos. M.	"	"	?	" "	Moderately soft.	"	..	..	..	..	..	+	..	..	..	0.769	0.233
P. 21.	10 mos. F.	"	"	?	" "	Moderately soft.	"	..	..	..	..	..	+	..	..	..	0.846	0.241
P. 17.	10 mos. M.	"	"	?	Yellow-red, transluc.	Moderate	Visible	..	..	..	..	+	..	..	..	..	1.046	0.279
P. 7.	10 mos. F.	"	"	?	" " "	"	"	..	..	..	..	+	..	..	..	..	1.158	0.291
P. 16.	9 mos. F.	"	"	?	Clear yellow-red	Firm	"	..	..	+	..	..	..	..	..	..	1.230	0.337
P. 6.	10 mos. M.	"	"	?	" " "	"	Normal.	+	..	..	..	..	..	..	..	..	1.538	0.425
P. 18.	10 mos M	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.538	0.553
P. 5.	10 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.938	0.523
P. 19.	11 mos. M.	"	"	?	" " "	"	"	..	+	..	..	..	..	..	..	..	1.938	0.557
P. 25.	9 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.938	0.596
P. 12.	10 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.938	0.599
P. 20.	10 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.938	0.603
P. 4.	10 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.984	0.774
P. 26.	10 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	1.997	0.601
P. 10.	10 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	2.307	0.783
P. 23.	8 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	2.517	0.587
P. 14.	8 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	2.615	1.071
P. 11.	8 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	2.768	0.905
P. 9.	8 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	2.768	0.940
P. 8.	2 yrs. F.	"	?	?	Pale yellow, transluc.	"	"	+	..	..	..	..	..	..	..	..	2.768	0.805
P. 1.	10 mos. M.	"	Iowa	?	Clear yellow-red	"	"	..	+	..	..	..	..	..	..	..	3.230	1.121
P. 15.	8 mos M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	3.691	1.220
P. 3.	10 mos. M.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	3.691	1.456
P. 22.	10 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	3.728	1.140
P. 13.	8 mos. F.	"	"	?	" " "	"	"	+	..	..	..	..	..	..	..	..	4.154	1.298

*Age estimated by butchers.

TABLE 12.—CATTLE THYROIDS

General.					Gross.				Microscopical.									Chemical.	
Case. No.	Age.	Sex.	Condition.	Locality.	Weight of Glands in gms.	Color.	Consistency.	Colloid.	Normal.	Colloid.	Normal-Early.	Colloid-Early.	Early.	Early-Moderate.	Moderate.	Moderate-Marked.	Marked.	Iodin, per gm., Dried.	Iodin, per gm., Fresh.
C. 34.	Young	steer.*	Good	Northern Ohio.	41	Opaque, pale brown.	Soft	Absent	..	..	..	..	..	..	..	.	+	0.077	0.016
C. 36.	"	"	"	Northern Ohio.	53	Very pale brown	"	"	..	..	..	..	..	..	..	..	+	0.154	0.031
C. 29.	Calf,	female.	Poor	Michigan	370	" " "	"	"	..	..	..	..	..	.	..	..	+	0.215	0.042
C. 30.	Young	steer.	Good	Northern Ohio.	39	" " "	"	"	..	..	..	..	..	..	..	..	+	0.231	0.052
C. 35.	"	"	"	Northern Ohio.	13	Dark brown-red	Moderate	Visible	..	..	..	..	..	..	..	..	+	0.270	0.062
C. 40.	"	"	"	Northern Ohio.	27	Brown red	"	"	..	..	..	..	..	+	..	..	..	0.969	0.205
C. 33.	"	"	"	Northern Ohio.	17	Dark brown-red	"	"	..	..	..	..	..	+	..	..	..	0.969	0.205
C. 31.	"	"	"	Northern Ohio.	17	" " "	"	"	..	..	.	..	..	+	..	..	..	1.030	0.222
C. 37.	"	"	"	Northern Ohio.	16	Translucent, brown-red.	"	"	..	..	..	..	..	+	..	..	..	1.000	0.248
C. 38.	"	"	"	Northern Ohio.	19	Pale brown, translucent.	Firm	"	..	..	..	..	..	+	..	..	..	1.030	0.252
C. 39.	"	"	"	Northern Ohio.	16	Pale brown, translucent.	"	Normal	..	..	..	..	+	..	..	..	..	1.123	0.314
C. 32.	"	"	"	Northern Ohio.	13	Brown red, translucent.	"	"	..	..	..	..	+	..	..	..	..	1.630	0.456
C. 65.	"	"	"	Northern Ohio.	12	Brown red, translucent.	"	"	..	..	+	..	..	.	..	..	..	2.153	0.482
C. 46.	"	"	"	Texas	12	Dark brown-red, translucent.	"	"	..	..	+	..	..	..	..	..	..	2.000	0.585
C. 51.	"	"	"	"	13	Pale brown-red, translucent.	"	"	..	..	..	..	+	..	..	..	..	2.186	0.615
C. 45.	"	"	"	"	13	Very pale yellow brown, transluc.	"	"	..	..	+	..	..	..	..	..	..	2 076	0.617
C. 48.	"	"	"	"	12	Pale yellow brown, translucent.	"	"	..	..	+	..	..	..	..	..	..	2.307	0.653
C. 64.	"	"	"	Northern Ohio.	13	Pale yellow brown, translucent.	"	"	..	..	+	..	..	..	..	..	..	2.615	0.664
C. 41.	Young	bull	"	Texas†	11.5	Pale yellow brown, translucent.	"	"	.	..	+	..	..	..	..	..	..	2.676	0 666
C. 42.	Young	steer.	"	"	12	Pale yellow brown, translucent.	"	"	..	..	+	..	..	..	..	..	..	2.384	0.726
C. 47.	"	"	"	"	11	Yellow-brown, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.730	0.892
C. 44.	"	"	"	"	15	Pale brown, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.922	0.901
C. 43.	"	"	"	"	11	Pale brown, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.937	0 952
C. 49.	"	"	"	"	11	Pale brown, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.107	0.988
C. 52.	"	"	"	"	12	Brown red, translucent.	"	"	+	..	..	..	..	.	..	..	..	3.091	0.992
C. 57.	"	"	"	"	12	Pale yellow, translucent.	"	"	+	..	..	..	.	..	..	..	..	3.254	1.020
C. 56.	"	"	"	"	11	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.537	1.039
C. 63.	"	"	"	"	11	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.230	1.040
C. 55.	"	"	"	"	12	Pale yellow, translucent.	"	"	+	.	..	..	..	..	..	..	..	3.230	1.069
C. 50.	"	"	"	"	14	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.384	1.133
C. 62.	"	"	"	"	12	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.630	1.152
C. 61.	"	"	"	"	12	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.630	1.161
C. 60.	"	"	"	"	11	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.230	1.208
C. 58.	"	"	"	"	12	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.999	1.215
C. 53.	"	"	"	"	13	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.999	1.292
C. 54.	"	"	"	"	11	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	4.153	1.347
C. 59.	"	"	"	"	11	Pale yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	4.768	1.592

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*i.e. 3 to 5 yrs. as estimated by cattlemen.
†General term among cattlemen, meaning any part of Great Plains.

TABLE 13.—SHEEP THYROIDS

General.				Gross.				Microscopical.									Chemical.	
Case No.	Age. Sex.	Condition.	Locality.	Weight in gms.	Color.	Consistency.	Colloid.	Normal.	Colloid.	Normal-Early.	Colloid-Early.	Early.	Early-Moderate.	Moderate.	Moderate-Marked.	Marked.	Iodin, per gm., Dried.	Iodin, per gm., Fresh.
S. 33.	F 8 mos.	Good	Seville, Ohio.	95.0	Gray red, translucent.	Soft.	Visible.	..	..	..	..	..	..	..	..	+	0.000	0.000
S. 37.	M. 10 mos.	"	Seville, Ohio.	115.0	Gray red, opaque	"	None	..	..	..	..	..	..	..	..	+	0.000	0.000
S. 39.	M. 9 mos.	"	Seville, Ohio.	85.0	" " "	"	"	..	..	..	..	..	..	..	..	+	0.000	0.000
S. 45.	M. 8 mos.	"	Seville, Ohio.	55.0	" " "	"	"		..	..	..	..	..	..	..	+	0.000	0.000
S. 20.	? 8 mos.	"	?	110.0	" " "	"	"	..	..	..	..	..	..	..	..	+	0.000	0.000
S. 36.	M. 9 mos.	"	Seville, Ohio.	120.0	Gray, translucent	"	Visible	..	..	..	..	..	..	..	+	..	0.000	0.000
S. 38.	M. 10 mos.	"	Seville, Ohio.	130.0	" "	"	"	..	..	..	..	..	..	..	+	..	0.000	0.000
S. 34.	F. 9 mos.	"	Seville, Ohio.	98.0	" "	"	"	..	..	..	..	..	..	..	+	..	0.024	0.003
S 35.	F. 9 mos.	"	Seville, Ohio.	110.0	" "	"	"	..	..	..	..	..	..	..	+	..	0.040	0.005
S. 59.	? 1 yr.	"	?	6.0	Opaque, red, granular.	"	None	..	..	..	..	..	..	..	..	+	0 036	0.006
S. 21.	M. 1 yr.	"	?	64.0	Opaque, red, granular.	"	Visible	..	..	..	..	..	..	..	+	..	0.092	0.014
S. 49.	F. 8 mos.	"	?	48 0	Opaque, red, granular,	"	"	..	..	..	..	..	..	+	..	..	0.400	0.091
S. 47.	M. 9 mos.	"	?	6.0	Red-gray, translucent.	Moderate	"	..	..	..	..	..	+	..	..	..	0.548	0.131
S. 32.	F. 4 yrs.	Fair.	?	370.0	Red-yellow, translucent.	Firm	Normal.	..	..	..	+	..	..	..	..	..	0.461	0.138
S. 43.	F. 5 yrs.	"	?	15.0	Red-yellow, translucent.	"	"	..	.	+	..	..	..	..	..	..	0.677	0.176
S. 51.	M. 9 mos.	Good	?	18.0	Red-yellow, translucent.	"	Visible	..	..	..	+	..	..	..	..	..	0.923	0.201
S. 50.	M. 9 mos.	"	?	16.0	Red-yellow, translucent.	"	"	..	..	..	+	..	..	..	..	..	0.784	0.202
S. 46.	F. 5 yrs.	Fair,	?	25.0	Clear yellow, translucent.	"	Normal,	..	..	..	+	..	..	..	..	..	1.000	0.282
S. 52.	? 1 yr.	Good	?	5.9	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	1.260	0.308
S. 53.	? 1 yr.	"	?	6.7	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	1.247	0.313
S. 55	? 1 yr.	"	?	6.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	1 425	0.365
S. 48.	F. 9 mos.	Fair.	?	5.9	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	1.602	0.405
S. 63	F. 3 yrs.	Good	?	8.0	Clear yellow, trans lucent.	"	"	+	.	..	..	..	..	..	..	..	1.615	0.430
S. 60a	M. 2 yrs.	"	?	58 0	Clear yellow, translucent,	"	"	..	+	..	..	..	..	..	..	..	1.769	0.455
S. 58.	? 1 yr.	"	?	4.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	1.812	0.468
S. 60	F. 3 yrs.	Fair.	Northern Ohio.	8.0	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.153	0.564
S. 61.	F. 3 yrs.	"	Northern Ohio.	8.5	Clear yellow, translucent.	"	"	+	..	..	.	..	..	..	..	..	2.288	0.582
S. 62.	F. 4 yrs.	"	Northern Ohio.	8.0	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.153	0.608
S. 65.	F. 4 yrs.	"	Northern Ohio.	8.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.392	0.694
S. 44.	F. 4 yrs.	"	?	6.0	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.250	0.727
S. 67.	? 1 yr.	"	?	7.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.644	0.735
S. 57.	? 1 yr.	"	?	5.4	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3 292	0.823
S. 70.	F. 4 yrs.	"	Northern Ohio.	7.0	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.054	0.861
S. 69.	F. 3 yrs.	"	Northern Ohio.	8.0	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.058	0.872
S. 66	F. 3 yrs.	"	Northern Ohio.	7.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	3.150	0.872
S. 54.	? 1 yr.	Good	?	6.55	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	2.500	0.890
S. 64	? 1 yr.	"	Northern Ohio.	8.0	Clear yellow, translucent.	"	"	..	+	..	..	..	..	..	..	..	3.691	0.974
S. 19	M. 2 yrs.	Excellent.	?	52.0	Clear yellow, translucent.	"	"	..	+	..	..	..	..	..	..	..	3.529	1.027
S. 56	M. 1 yr.	Good	?	6.4	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	4.368	1.200
S. 68.	M. 10 mos.	"	Northern Ohio.	7.5	Clear yellow, translucent.	"	"	+	..	..	..	..	..	..	..	..	4.614	1.318

methods, the colloid series will contain sufficient gradations of the hyperplasias to parallel the normal series throughout and will be discussed with equal emphasis.

These two groups of colloid glands suffice, however, to illustrate, first, the fact that pure colloid glands of the different animals have iodin contents very closely approaching those of normal glands, and, second, that colloid-early glandular hyperplasias have iodin contents similarly close to those with normal-early glandular hyperplasias. We believe that if all the conditions (diet, etc.) could be strictly controlled the iodin content of colloid glands would absolutely parallel those of normal glands and that a like parallelism would be seen throughout the gradations of hyperplasia of both the normal and colloid series.

The probable reasons why we rarely obtain colloid glands in sheep, cattle and hogs are (1) that they are killed at an age when the natural occurrence of colloid glands is rare, and (2) that the conditions of life (as regards habits, food and locality) are more constant than obtain for man or dogs.

So striking a uniformity in the anatomic changes for widely different animals can not be without significance. It suggests that the etiologic factor or factors in the production of thyroid hyperplasia (goiter) are probably the same in all these animals. The constant relation between structure and iodin content suggests that iodin is a common factor in all these animals.

It seems fair to infer from this comparative study of anatomic structure and iodin content that iodin is a very important factor, acting in the same direction and manner in all classes of animals in which hyperplasias (goiterous changes) are observed, and that, therefore, for a general study of goiter, any of the animals mentioned may be used as a basis, and the results be applicable to man.

NOTE.—In conclusion we wish to thank Professors Torald Sollmann and G. N. Stewart for their careful criticisms and suggestions.